

Cervical Vertebral Maturation as a Valid Predictor of Growth

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List of Abbreviations

ANOVA	Analysis of Variance
BMI	Body Mass Index
CI	Confidence Interval
Co	Condylion
CVM	Cervical Vertebral Maturation
Gn	Gnathion
Go	Gonion
ICC	Intra-class Correlation Coefficient
PIL	Patient Information Leaflet
REC	Research Ethics Committee
PGs	Post graduate students
SMIs	Skeletal Maturational Indicators
StRs	Specialist Registrars
WHO	World Health Organisation

Abstract

Cervical Vertebral Maturation as a Valid Predictor of Growth

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Objectives: The primary objective was to assess if a correlation exists between CVM and statural height growth velocity. The secondary objective was to assess if a correlation exists between CVM and mandibular growth velocity.

Design/Setting: A prospective longitudinal study undertaken at Liverpool University.

Subjects: Participants were aged between 8-18 years, of either gender and enrolled from the orthodontic waiting list at Liverpool University Dental Hospital.

Methods: Standing height was measured every 6 weeks with subjects barefoot and in natural head position. Lateral cephalograms were taken at the start of treatment, on completing functional appliance therapy and prior to debond. Lateral Cephalograms were traced and analysed digitally. A random 10% sample was retraced to assess the method error and reproducibility. Mandibular growth was assessed using the area of the triangle condylion-gnathion-gonion to ensure data were comparable with previous research. Intra- and inter-observer reliability of CVM staging, cephalometric and statural height measurements were assessed using Cohen's weighted kappa, intra-class correlation coefficient (ICC), and Bland and Altman plots respectively. ANOVA was used to test for statistically significant differences between statural height velocity and mandibular growth at CVM stages.

Informed consent was obtained from parents/patients as soon as was reasonably possible after ethical approval was obtained. All participants underwent radiographic exposure in line with normal clinical practice; no additional exposure was required for this study.

Reliability and Calibration: SH was calibrated in the assessment of CVM stage, to JH who had been calibrated in a previous study (Rainey, 2015). The intra-observer reliability of CVM index was perfect agreement (Kw 1). Inter-examiner reliability of CVM index was also perfect agreement (Kw 0.83, 0.96). Intra- and Inter-observer reliability for statural height measurements were excellent (ICC: 0.986-0.997). Intra-observer reliability of cephalometric measurements was good (ICC: 0.85-0.93).

Results: 108 participants were included for analysis. The peak in statural height growth velocity occurred at CVM stage 3 ($p=0.001$). The peak in mandibular growth occurred at CVM stage 3, although this was not statistically significant.

CVM Stage	Number of patients	Mean annualized growth rate (cm y^{-1})	Standard deviation (cm y^{-1})
1 & 2	14	4.51	2.71
3	22	9.39	4.44
4	33	5.00	2.33
5 & 6	39	1.56	2.34
Total	108	4.59	4.06

Table 1: Mean Annualised Growth Rate by CVM Stage (cm/yr)

CVM Stage	Area of Triangle Co-Go-Gn (cm $^2y^{-1}$)	Condylion-Gnathion (cm y^{-1})	Gnathion-Gonion (cm y^{-1})	Gonion-Condylion (cm y^{-1})
1 & 2 (N= 5)	0.19	0.38	0.13	0.19
3 (N= 11)	0.45	0.54	0.17	0.45
4 (N= 8)	0.45	0.54	0.16	0.45
5 & 6 (N= 12)	0.26	0.26	0.08	0.26

Table 2: Mean change in annualized area of triangle Co-Go-Gn and linear measurements Co-Gn, Gn-Go, Go-Co.

Conclusions: The findings of this study demonstrate that CVM staging is valid for identifying the pubertal peak in statural height. The peak in mandibular growth as assessed by the triangle Co-Go-Gn occurred at CVM Stage 3, but this was not statistically significant.

Ethical approval was granted from Liverpool East Research Ethics Committee on 30th October 2013 with reference number 13/NW/0408 and protocol number UoL000751.

Chapter 1: Introduction

Knowledge of craniofacial growth and development is fundamental to the comprehensive and successful management of orthodontic patients.¹ It plays a vital role in the diagnosis, treatment planning, result and overall stability of the patients' outcome.¹

Certain aspects of orthodontic treatment are achieved most effectively and efficiently when facial growth is occurring at a rapid rate, such as growth modification using functional appliances, reducing an overbite, and distalising buccal segments.²⁻⁵ During puberty, the rate of growth is faster than at any other time after infancy and is when orthodontic treatment is usually undertaken.⁶ It would therefore be helpful if the phases of treatment that relied on growth could be carried out during this period.

Numerous methods have been investigated to identify the stage of growth and development and predict both the timing and potential of this growth.⁷⁻¹⁸ These include chronological age, dental age,⁷⁻⁹ menarche and voice changes,^{10, 11} standing height,^{12, 13} skeletal maturation of the hand and wrist,^{7, 8, 11, 14} and cervical vertebral maturation (CVM).¹⁵⁻¹⁸

However, none of these methods have demonstrated a strong enough correlation to growth with the exception of skeletal age of hand wrist radiographs and cervical vertebral maturation.^{5, 7, 19-24} The principle of using skeletal maturity in order to determine the most appropriate time to carry out orthodontic treatment has varied in popularity, but has always required additional radiation exposure and additional skills for the orthodontist to interpret the hand wrist radiographs.²⁵ As a result, alternatives to hand wrist radiographs were sought using investigations which were more common place in orthodontics and more familiar to the orthodontist to facilitate interpretation.²⁶ CVM is an alternative method to hand wrist radiographs that has been shown to be reliable^{19, 20, 27-29} and does not require the use of additional radiation.²⁰ This study aims to investigate the validity of CVM as a predictor of standing height and mandibular length.

Chapter 2: Literature Review

2.1: Introduction

An early approach to predicting facial growth and its extent was to compare the inherited characteristics between siblings and parents.³⁰ Numerous authors, but all with very little success, investigated this approach.³⁰⁻³² A review of the literature showed that neither chronological age nor dental development stages display enough correlation with individual maturational development to provide an adequate basis for treatment timing.^{33, 34} Many studies showed that there is great variation in the onset and extent of somatic growth at the initial stages of adolescence.^{12, 13, 35-37} Thus, it is argued that physiological measures of maturity, rather than chronological measures, should be preferred for assessing individual growth and development,¹³ so research then focused on biological indicators such as statural height, skeletal maturation of the hand and wrist and cervical vertebral maturation. Maturational variations have been shown to be closely associated with variations in the onset and amount of growth.^{5, 38}

The importance of knowing and being able to predict when the peak in growth will occur and has passed can readily be appreciated when different orthodontic treatment modalities are considered. Regarding class 2 skeletal relationships, the main aim of functional appliances is to induce growth modification and lengthening of the mandible by stimulating growth at the condylar cartilage.^{4, 39} How successful the functional appliances are will depend on the amount of growth at the condylar cartilage, which in turn depends on the growth velocity of patient.⁴ In contrast, treatment aimed at enhancing or restraining maxillary growth is more efficient when tackled before the adolescent growth spurt.^{15, 40} However, it is recommended that the best time for correction of mandibular prognathism is after the completion of mandibular growth.²⁵ Thus, the importance of information regarding growth timing and potential is invaluable in order to obtain optimal orthodontic treatment results.

2.2: Background and Rationale

Knowledge regarding the timing and extent of growth for orthodontic patients is essential in order to manage them optimally and successfully, particularly in patients with skeletal discrepancies.¹ Previously, numerous methods have been used in order to attempt to assess the growth and development stage of orthodontic patients.^{5, 7-17} However, limitations associated with previous methods of assessing growth have led to continued efforts to find a reliable and valid diagnostic tool that will accurately assess the stage of growth and development, in a manner that is easy to apply by the orthodontic profession.

The CVM staging index¹⁵ assesses the shape of the cervical vertebrae visible on a standard lateral cephalogram and uses this to predict the stage of growth and development of the patient. Whilst many studies have looked into the validity of this index,^{15-17, 19, 24, 41-48} most have used historical samples, and have been retrospective. Methodological flaws, as well as sampling issues, means that the validity of the CVM method is yet to be shown in a contemporary population sample in a prospective manner.

2.3: Prediction of Growth and Development

2.3.1: Chronological Age

Often, the initiation of active orthodontic treatment is determined by the age of the patient as well as the stage of dental development.⁴⁹ Chronological age has been shown to be an unreliable factor for establishing the stage of skeletal development;^{5, 7, 50} in addition, many authors have concluded that chronological age does not necessarily correlate with maturational age.^{5, 50} Furthermore, many studies have demonstrated significant differences in the timing of skeletal growth and development between males and females during adolescence.^{13, 50, 51}

Baccetti et al. concluded that chronological age showed a very low diagnostic value for the detection of the onset of the adolescent peak in skeletal maturation in both males and females.¹⁵

Due to the large inter-individual variation that chronological age shows when correlated with developmental events around puberty, it is recommended that a biological indicator is used when evaluating individual skeletal maturity.¹³ Franchi et al.⁵² assessed the stage of dental development and its relationship to the pubertal growth spurt. This study also provided data demonstrating the variability of chronological age with respect to onset of the pubertal peak in skeletal maturation, with the age range ranging from 8 years to 14 years and 6 months.⁵² This wide variability emphasizes that there is little value in using chronological age as a tool for evaluating skeletal growth and maturation, especially with regards to orthodontic treatment planning. However, Beit et al. have recently suggested that chronological age may be as good as using other methods of assessing skeletal maturity.⁴⁹

2.3.2: Dental Development

For many years, there has been debate regarding the relationship between the stage of development of the dentition and skeletal maturity. The literature reported inconclusive results with some reporting a high correlation between dental and skeletal ages^{22, 53} and some low and insignificant correlations.^{21, 54-56}

Sierra suggested that although previous studies had shown low correlation between skeletal maturation and dental eruption or calcification, that this may have been due to using ossification centres that exhibited a wide variation in their onset.⁵⁴ She therefore investigated the correlation using ossification centres that showed low variability in their onset, specifically the calcification of the mandibular canine, and concluded this showed a significant correlation between skeletal maturity and maturity of the dentition.⁵⁴

Most of the studies in the literature focus on the calcification or eruption of specific teeth, in particular, the mandibular permanent canines and the second permanent molars with a wide range of correlations reported between the point of calcification or eruption of teeth and skeletal maturation.^{7, 21, 50, 57, 58} No correlation has been shown between stage of dental development and mandibular growth⁵² and only weak correlations with the peak in statural height have been shown.^{7, 50}

Other studies, rather than focusing on the calcification or eruption of specific teeth, have looked at the phases of the dentition. The phases used were mostly the four classic developmental stages as defined by Bjork,⁵⁹ the early mixed, the intermediate mixed, the late mixed and the early permanent phases. Franchi et al.⁵² found that the early mixed dentition was a useful indicator for the pre-pubertal stage of skeletal maturity as it scored highly as a diagnostic performance indicator for cervical stage 1 when correlated with CVM staging. The shedding of the deciduous incisors and eruption of the permanent incisors and first molars was concluded to be a powerful indicator of the pre-pubertal stage.⁵² It has been suggested previously that this stage may be the most appropriate and ideal time to start treatment aimed at altering maxillary growth with rapid maxillary expansion and the use of a facemask.⁴² However, in the same study, it was concluded that all the other phases of the dentition were not reliable indicators in determining the onset of the pubertal growth spurt which the authors take to be cervical vertebrae stage 3.⁵² When compared to a physiological indicator of skeletal maturity (such as the CVM or hand wrist maturation methods), dental development stage performs poorly in the evaluation of the onset of the pubertal growth spurt.

2.3.3: Sexual Development

The onset of puberty varies according to gender, population, and environment and shows a great deal of individual variation.⁷ Bjork and Helm showed that there was a close association between the age at the maximum increase in statural height and for girls, the age at the menarche.⁷

Hagg and Taranger however, showed that the peak in growth velocity preceded menarche.¹⁰ It was later suggested that the menarche follows the peak growth spurt by an average of 1.28 years.⁵¹ Although menarche can therefore give an indication of the post-pubertal peak, its presence indicates that the orthodontist has missed the pubertal growth peak, which for certain treatment modalities, is of little use. Hagg and Taranger also showed that with boys, once voice changes were complete, this indicated that growth was decelerating.¹⁰ Whilst useful to know that no significant further growth is likely to occur, it has limited use in predicting the event of peak growth velocity.

In contrast, it has been shown that development of the testes in boys precedes the peak growth spurt and that this is a reliable indicator for predicting a forthcoming growth spurt.^{60, 61}

Despite the features that do show a strong correlation with the peak growth spurt, a valid question is how appropriate is it to attempt to ascertain this information from the orthodontic patient? Often patients feel sensitive about disclosing personal medical and social information that is routinely obtained, thus a line of questioning regarding pubertal development, such as the menarche and the development of the testes, is certain to cause embarrassment and may meet barriers to ascertaining the information required. As such, these features of sexual development may be deemed inappropriate, for an orthodontist, to ascertain and use to predict growth.

2.3.4: Statural Height

Expected height, weight, Body Mass Index (BMI) and height velocity for boys and girls are displayed in growth charts. Various growth charts have been developed for assessment of children in the UK, which follow the development of children from birth to adulthood. They can be used, either for assessment and monitoring of an individual, or for screening a population. They are based on longitudinal or cross-sectional population data. Both types of data have their methodological issues. Longitudinal data suffers from the influence of time-lag bias and is only generalisable to the population from which the data were derived. Cross-sectional charts are not strictly valid for monitoring growth over time. The Royal College of Paediatrics and Child Health convened in 2002,⁶² with an expert group to provide guidance on the validity of available growth charts, including Tanner-Whitehouse,⁶³ Gairdner-Pearson,⁶⁴ Buckler-Tanner⁶⁵ and the UK 1990 growth references.⁶⁶ They concluded that the 'UK 1990' reference is the only suitable reference that can be recommended'.⁶²

More recently, the World Health Organisation has conducted a multicentre growth study to develop growth standards.^{67, 68} The WHO growth standards followed how children grew in

ideal conditions, from birth to two years. They were based on children who were breast fed, in different countries around the world. This study compared the UK1990 and WHO data from 0-24 months; the WHO standard shows a slower rate of weight gain from 4-24 months for infants who were breast-fed only compared with mixed formula fed infants. This slower weight gain has been shown to be indicative of a reduced risk of obesity later in life. From an ethnic point of view, the WHO growth standard may be more applicable to the current multinational UK population compared to the UK 1990 population, however, most infants in the UK, regardless of ethnic origin, are mixed or formula fed. This has led to the amalgamation of the UK 1990 from 24 months to adulthood, and the WHO standards, from 0-24 months,⁶⁹ to form the current recommended growth charts for use in the UK.

2.3.5: Somatic Development

The timing of the growth spurt varies in different parts of the body, but for most facial dimensions, peak growth velocities occur at approximately the same time as in peak height velocity.^{33, 34} The peak statural height spurt occurs, on average at 12 years for girls and 14 years for boys with a standard deviation of 1 year in both genders.⁵

Disagreement exists in the literature regarding the evidence of a correlation between standing height and dentofacial growth.^{11,22,54,55} One body of researchers suggest that dentofacial growth is strongly correlated with standing height,^{11, 22, 55} whilst the other body reports a weak or insignificant correlation.⁵⁴ It has been reported that the peak dentofacial growth velocity is reached after the peak statural body height.⁷⁰ In contrast, Hunter in addition to other authors found that dentofacial growth velocity and statural height velocity coincided.^{13, 71} Nevertheless, flaws in the methodology, as well as different definitions being used and selection bias, means that there is little strong evidence to support or refute the argument either way.

Summarising the discussion, Van der Beek,⁷² argues that comparisons are possible and measurable, as long as specific aspects of a growth curve, such as the onset and duration, are compared and correlated statistically to produce valid comparisons and conclusions.

Mitani and Sato⁷³ looked at the relationship between mandibular growth and numerous variables, including standing height, cervical vertebrae and hand-wrist bone maturation, in an attempt to look at a potential relationship between mandibular growth to other clinical variables during puberty. The conclusion of their study was that there was large variability in the onset and extent of the growth spurt between all the variables. Mandibular growth interestingly displayed the most variability and the authors concluded that orthodontists should be aware of the 'unpredictable and random' variation in mandibular growth, both the

onset and the magnitude;⁷³ this having an effect on retention and stability as well as active treatment.

Plotting height measurements against age would produce a line that continues to increase then level off, as statural height no longer increases. It can be difficult to recognise when the peak in statural height is from a serially plotted curve therefore most studies look at peak height velocity. Plotting the height velocity means that a growth curve easily illustrates the peak spurt, demonstrated by the highest point on the curve as illustrated by the graph in Figure 2.1. From Figure 2.1, it can be seen that after birth, the rate of growth decelerates with the exception of two phases. One is at approximately 6 or 7 years old but this is a relatively inconsistent phase. After this, a slowly decelerating phase exists until the second pubertal growth spurt occurs during adolescence. During puberty, the rate of growth is at its highest since the postnatal period, and an accelerated phase of increased growth occurs, often referred to as the 'circumpubertal growth spurt'; and is when orthodontic treatment is normally undertaken. In both males and females, the Peak Height Velocity (PHV) is seen approximately two years after the onset of the pubertal growth phase. Growth velocity then slows to adult levels. The onset, duration and extent of growth can vary significantly among individuals of the same chronological age.⁷⁴

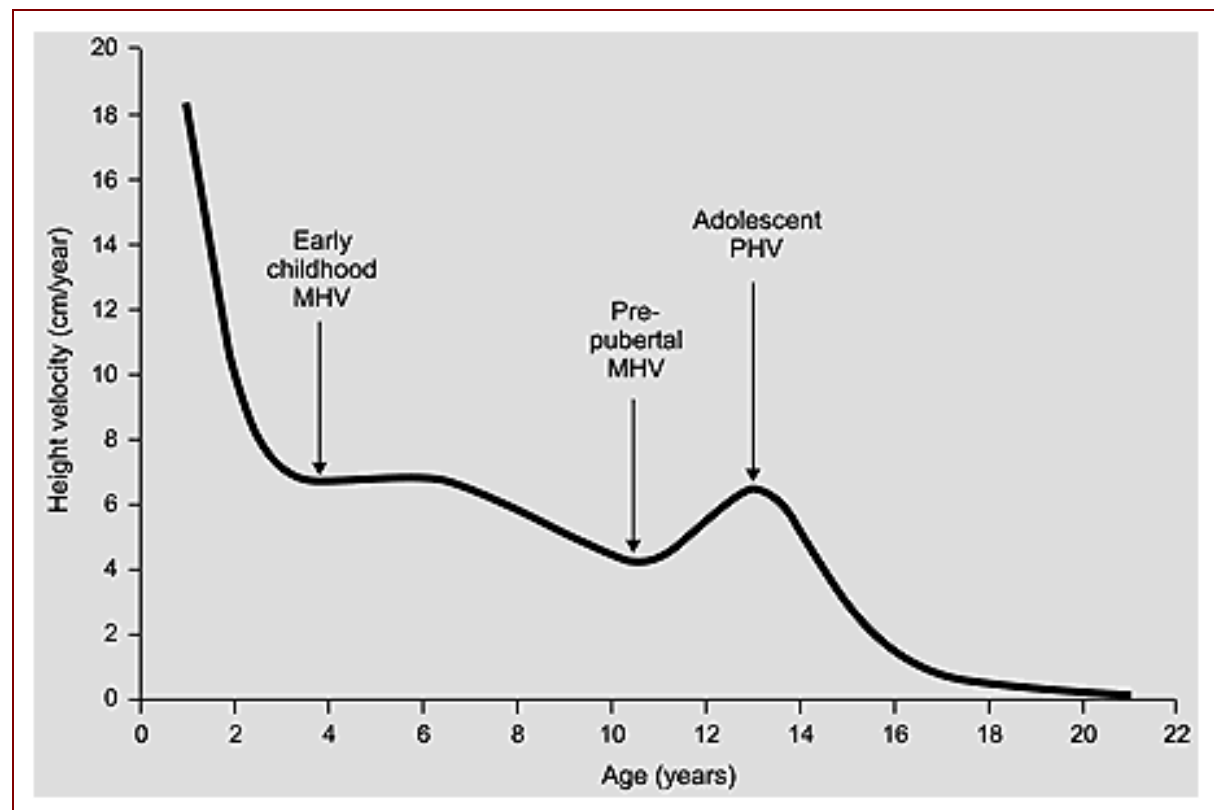


Figure 2.1: Average height velocity growth curve throughout stages of life from infancy to adulthood (MHV: minimum height velocity, PHV: peak height velocity). Adapted from Siervogel *et al.*⁶

Statural height growth velocity is recognized as a useful measure of an individual's growth. However, serious limitations exist regarding the practical use of these data for the prediction of future growth by orthodontists, as the peak in growth velocity may only be recognised after it has occurred, i.e. on a downward curve of a growth chart. The irregularity of the plotted curve makes it difficult to identify when the peak or spurt in growth is until it has passed. However, for the information to be useful, orthodontists would really need to know this information prior to this. Although the data would provide useful information that would allow the orthodontist to know that a patient has completed growth, perhaps in a case where there is a class III skeletal relationship, or where orthognathic surgery or implants were being considered, it would be of limited value in those cases where active growth is required to achieve the optimum treatment aims.

Sullivan described measuring statural height longitudinally as a method of predicting the pubertal growth spurt in preparation for starting orthodontic treatment.⁷⁵ He suggested routinely measuring standing height. The height velocity could then be calculated and plotted on a graph against age to give a height velocity chart. The point in a patient's development which anticipates the occurrence of the peak in height velocity is predicted based on criteria set out in templates, one for males and one for females, outlined by Sullivan in his paper.⁷⁵

However, obtaining this information would necessitate orthodontists seeing potential patients for a significant period prior to commencing treatment.

Tanner developed an onlay chart as part of the Harpenden growth study, which was placed over the height velocity chart and allowed the operator to determine which growth chart the patient was following and from which predictions could be made.⁶⁰ However the limitations of this method include the Harpenden sample being historic and thus the data may not be applicable to the current population. Furthermore, the girls in the sample were in state care and many had emotional problems, which may have affected pubertal onset and restricted growth. The current growth charts have a supplemental guide for assessing pubertal stage using Tanner's stage of puberty, however, these require a patient interview regarding the development of secondary sex characteristics, which may be inappropriate for patients seeking orthodontic treatment.

Many authors have found a significant correlation between maturational stages from hand-wrist radiographs and changes in standing height.³⁸ Most of these studies compared skeletal maturation stages with one or many stages of growth such as the onset, peak, deceleration or maximum growth velocity. The majority of studies have placed the greatest significance on correlations found close to the time of maximum growth velocity.^{7, 38}

In summary, many authors showed a high level of correlation of facial growth with general body growth (stature, standing height).³³ In contrast, other authors argued that there was a low level of association.⁷⁶ Of those who concluded that there was a strong correlation, some suggested that the facial growth peak was coincident with a standing height peak,^{13, 77} whereas some suggested that the peak of facial growth usually occurs slightly later than the statural height peak.^{35, 78} Peak growth velocity is a useful longitudinal measure of an individual's growth pattern but has limited use with regards to predicting the timing or extent of future growth. Longitudinal regular height assessment would be required to identify a higher velocity of growth, and despite this it may only be detected when the velocity curve begins to reduce thus, indicating that the peak in growth has been missed.⁷⁹

2.3.6: Skeletal Maturation

The degree of maturation of certain bones can be used to assess skeletal and general maturation and development. Distinct bony changes in hand wrist radiographs as well as the knee and cervical vertebrae have been described in order to assess a patient's skeletal age.

2.3.6.1: Hand-wrist Radiographs

Fishman developed an index using hand-wrist radiographs to evaluate skeletal maturity using a sample consisting of both longitudinal and cross-sectional groups.³⁸ The underlying idea behind this theory was that osseous changes in the hand and wrist were indicators of more general skeletal changes.

Looking at the previous work in the literature on which Fishman built, Greulich and Pyle first described an atlas method of predicting the skeletal age using hand wrist radiographs.¹⁴ The patient's radiograph was compared with a standard series of radiographs, selected to be representative of normal children at different skeletal ages. The skeletal age was taken to be that of the standard film that the radiograph in question matched most closely. A criticism of this method was that as different bones all mature at slightly different rates, it may be difficult to decide on one standard film to which it matches most closely.⁵

The Tanner and Whitehouse method used a weighted score designated to the stage of maturation of all 20 bones in the hand and wrist.⁸⁰ The composite score for the radiograph then determined the bone age.⁸⁰

At this point, few studies had discussed single bone stages as criteria of skeletal maturity. Bjork discussed the use of specific bone stages to indicate whether the growth spurt had passed or not.³⁴ However, Houston discussed the limitations of this method, arguing that the practical difficulties involved with serial observations will preclude its use in most clinical orthodontic situations.⁵ In addition, he argued that bone stages and ages have a huge

advantage in that a single radiograph can provide the information required.⁵ Although single bone stages can inform us whether the growth spurt has passed or not, they would not be useful in predicting the peak height velocity age.

The methodology for Fishman's study involved examining his sample in relation to specific maturational characteristics. Eleven discrete skeletal maturational indicators, (SMIs) covering the whole period of adolescent development, are found on six anatomical sites (shown in Figure 2.2) located on the thumb, middle and little fingers and radius using four stages of bone maturation³⁸ (shown in Figures 2.3 and 2.4).

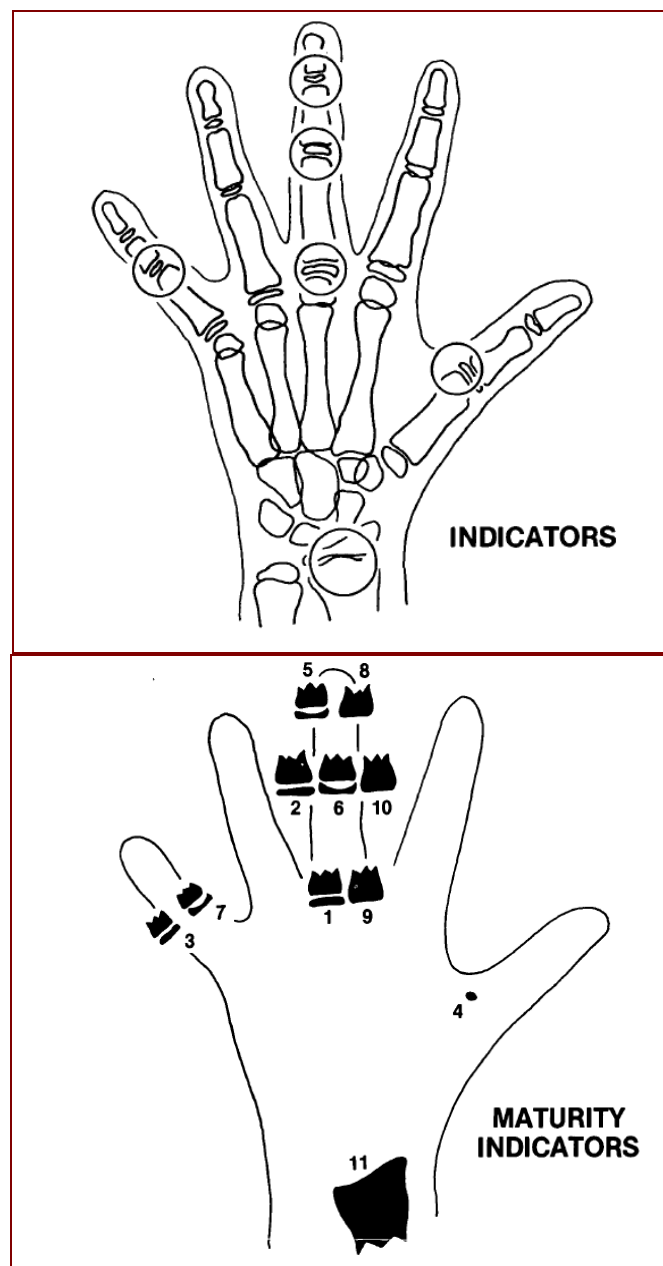


Figure 2.2: Sites of Skeletal Maturity Indicators. Adapted from Fishman³⁸

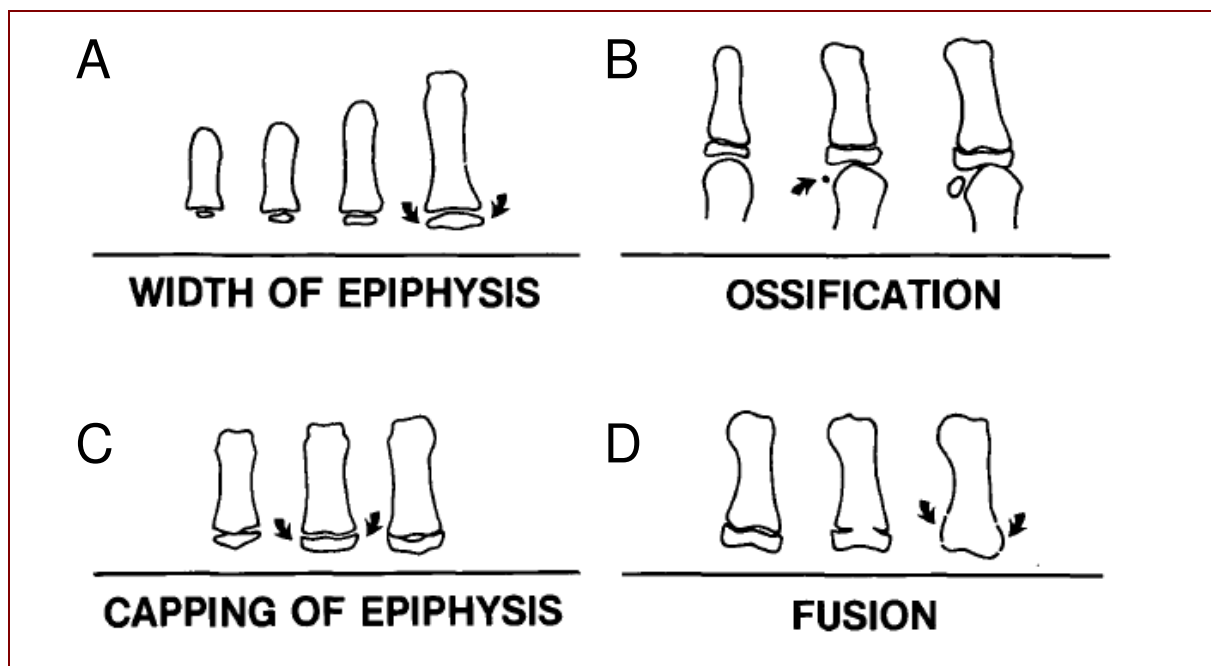


Figure 2.3: Radiographic Identification of Skeletal Maturity Indicators. A- Epiphysis equal in width to diaphysis B- Appearance of adductor sesamoid of the thumb C- Capping of epiphysis D- Fusion of epiphysis. Adapted from Fishman³⁸

The stages of maturation progress from widening of the epiphysis, ossification, capping of the epiphysis and fusion of the epiphysis and diaphysis and the SMI are shown in Figure 2.3.

Width of epiphysis as wide as diaphysis	Capping of epiphysis
1. Third finger -proximal phalanx	4. Third finger -distal phalanx
2. Third finger -middle phalanx	5. Third finger -middle phalanx
3. Fifth Finger- middle phalanx	6. Fifth Finger -middle phalanx
Ossification	Fusion of epiphysis and diaphysis
7. Adductor sesamoid of thumb	8. Third finger -distal phalanx
	9. Third finger -middle phalanx
	10. Fifth Finger -middle phalanx

Table 2.1: Individual Skeletal Maturity Indicators in chronological order. Adapted from Fishman³⁸

Poor correlation between dental, maturational and chronological ages means that maturational indicators are a more valid means of judging physiological development than chronological age or dental development which can be misleading.⁸¹ Adolescents display a huge variation in growth, showing differing onsets of acceleration of growth, and it is here when the merit of hand wrist radiographs becomes apparent.

However, the key limitations of the SMI index is that it requires an additional radiation dose for the orthodontic patient on top of the standard orthodontic diagnostic radiographs.²⁵ IRMER 2000 advises that the ionizing radiation dose must follow the principle of being as low as reasonably possible, and that clinicians should try to minimize the number of radiographs taken of patients, unless absolutely necessary.⁸² In addition to the extra radiation, the SMI index uses an anatomical area i.e. bones of the hand and wrist, that is not commonly studied in detail by orthodontists and thus it is not an area that they are skilled in interpreting. This may have implications for ease of use for the orthodontic or dental profession.⁴

Further critique of Fishman's work on skeletal maturation of hand wrist radiographs, was that although a longitudinal sample was used, allowing trends to be seen over time, it was a retrospective sample from the Denver Child Research Council.³⁸ This study was active from 1927 to 1967, so it started 55 years prior to the publication of Fishman's work. Retrospective studies carry a high level of bias, and there would have been no standardisation as to the purpose of the study. In addition, the paper states that not all the hand-wrist radiographs were available for each period; this may have led to further bias in the study due to incomplete data. The cross-sectional sample was of the population at the time, but no information was given on how the sample was selected, whether it was randomly selected or if it was a sample of convenience.

Despite these limitations, this study³⁸ presented a technique of skeletal maturation assessment using hand wrist radiographs to facilitate the objective evaluation of maturational development and has been a very popular method. It is still commonly used today by orthodontists around the world, although not in the UK.⁸³ It offers an organised and relatively simple technique to evaluate the maturation stage that is a more valid and reliable method than the use of chronological age or dental developmental stage.

2.3.6.2: Cervical Vertebral Maturation

The routine use of hand-wrist radiographs has recently been questioned due to ethical issues regarding the additional radiation to which patients are being exposed.²⁵ Recently, skeletal maturation assessment using cervical vertebrae maturation stages has gained in popularity due to its advantage of eliminating the need for additional radiation exposure, because the cervical vertebrae are already visible on the lateral cephalometric film that is frequently used to assist orthodontic diagnosis. Many studies in the literature have demonstrated the validity of the cervical vertebral maturation index to evaluate skeletal maturity instead of hand and wrist bones.^{19, 46-48} This method makes the evaluation of skeletal maturation easier and more applicable for orthodontists without the need to justify extra radiation to orthodontic patients.

There are a number of advantages of using the CVM staging method over other previously discussed methods of assessing maturity and growth, and it is this index on which this research project will be based. The next section (2.4) will focus in detail on cervical vertebral maturation staging index, its inception, developments, strengths and shortcomings reported in the literature.^{14-17, 19, 39, 84-88}

2.4: Development of Cervical Vertebral Maturation Index

2.4.1: Anatomy of Cervical Vertebrae

The cervical spine consists of the first seven vertebrae in the spinal column. The first two, named the atlas and the axis, respectively are unique in shape.⁸⁴ The third to the seventh vertebrae are similar in anatomy.⁸⁴ As the vertebrae mature, changes can be seen in distinct stages from birth until full growth has been reached.^{89, 90}

After endochondral ossification of the vertebral body is complete, periosteal apposition on the front and sides of the vertebral body provides the means of growth.^{85, 86} Todd and other authors were the first to measure the cervical vertebrae from lateral cephalograms, although they looked at the lower vertebrae.^{87, 88} Lamparski is thought to be the first author to study the change in shape and size of the upper vertebrae (second to sixth) to create maturational standards for the prediction of growth.¹⁷

2.4.2: Inception of Cervical Vertebral Maturation Theory

In 1972, Lamparski completed his unpublished thesis titled "Skeletal Age Assessment Utilizing Cervical Vertebrae".¹⁷ His aim was to determine whether the changes in maturation of the cervical vertebrae, seen on a standard orthodontic lateral cephalometric radiograph, could be used to evaluate the skeletal age of a patient. He used the method of Todd,⁹¹ which

had also been used by Greulich and Pyle,¹⁴ because at the time this method was the gold standard for determining skeletal ages. The cross-sectional sample was selected from the files of more than 500 Caucasian patients at the Orthodontic Department in the School of Dental Medicine, Pittsburgh, USA. Lateral cephalograms for a sample of 72 girls and 69 boys were used to determine the standards.

Maturity indicators were described and based on a selection of lateral cephalograms of a similar aged group of patients to those who were used as standards. The maturity indicators were observed changes that were demonstrated in all patients and signified a stage in development. To test the reliability and the validity of the standards, compared to the evaluations made from the wrist area, Pearson product moment correlation (r) and t tests for matched pairs were carried out. A sample of 25 boys and 25 girls who had lateral cephalograms and wrist films taken at the same time was used for this test.¹⁷ Lamparski concluded that there were no statistical differences between the maturation stage determined from the wrist and that determined from the cervical vertebrae and concluded that the cervical vertebrae could be used to predict skeletal age.¹⁷ He also found that the maturity markers were the same for males and females but that females matured earlier than males.¹⁷

The indicators of maturity that the study concluded to be valid were the development of concavities in the lower border of the vertebrae as well as increased height of the vertebral bodies. The vertebral canal's sagittal diameter and ossification of the vertebral ring were not found to be valid maturity indicators.¹⁷ Lamparski thus created maturational standards from C2 to C6, providing 6 stages of maturation based on the shape and lower borders of the cervical vertebrae.

2.4.3: Developments to initial Cervical Vertebral Maturation Index

Following on from Lamparski's work,¹⁷ Hassel and Farman¹⁹ looked at lateral cephalogram radiographs and hand-wrist radiographs of patients from the Bolton-Brush Growth Centre. In a retrospective study using this historical sample, they correlated the stages of maturation and development and also agreed that CVM was a valid assessment of growth potential. The study described six distinct phases of vertebral maturation for C2, C3 and C4 involving changes in the shape (wedge shaped, square or rectangular), the vertical and horizontal dimensions and the curvature of the lower border. The six phases they described are shown in Figure 2.5. The sample was randomly selected from patients in the Bolton Brush growth study,⁹² and consisted of 220 patients, split equally into males and females. Inter-operator error and intra-operator error were accounted for in the results and were both insignificant. A significant limitation of this study however, was the retrospective and historic nature of the

sample, which affects how representative and applicable it would be to the current population. Another limitation discussed by the authors was that fact that maturation is a continuous process, yet the use of the CVM Index requires a distinct stage to be denoted to the CVM, thus it may be difficult to assign a stage to borderline cases.

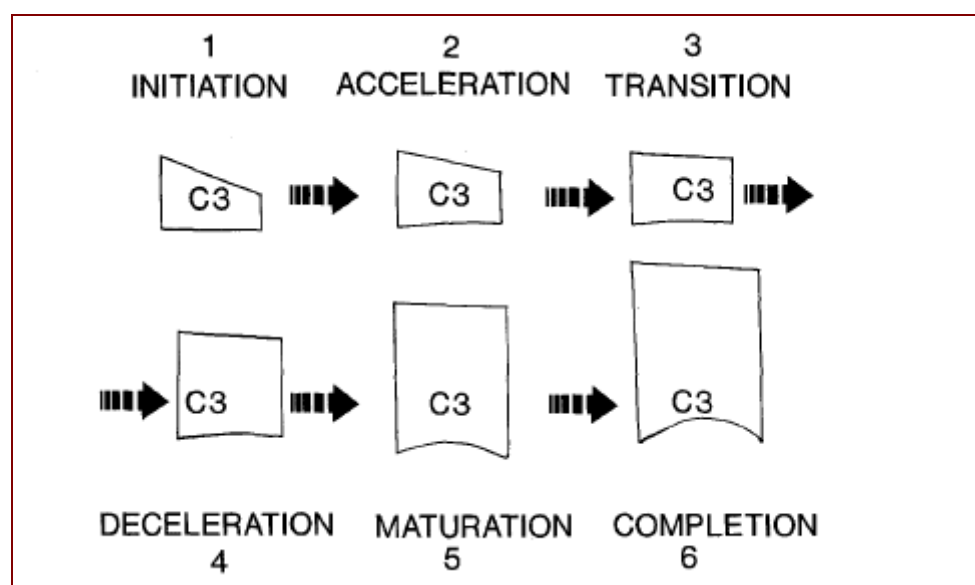


Figure 2.5: Cervical vertebral maturation indicators using C3 as a guide. Adapted from Hassel and Farman¹⁹

Hassel and Farman,¹⁹ Bacetti et al.,¹⁶ as well as Pancherz and Szyska³⁹ stated that the cervical vertebral analysis had a validity and reliability that was as comparably high as the hand-wrist skeletal age assessment.

Franchi, Baccetti and McNamara²⁰ undertook a study to assess the validity of the method of cervical vertebral maturation for the evaluation of skeletal maturity and identification of the pubertal peak in craniofacial growth. They concluded that the method was valid, and reported the greatest incremental change in body height took place between stage 3 (when a concavity develops in the lower border of the third vertebrae) and stage 4 (when a concavity develops in the lower border of the fourth vertebrae and all the bodies of the cervical vertebrae become rectangular) as shown in Figure 2.6. In addition, they reported that the peak change in statural height, that occurred between stage 3 and stage 4, was accompanied by the peak change in mandibular dimensions and position.²⁰ Although this study provided strong evidence to support the validity of the CVM method, the sample size was only 24 and was taken retrospectively from the University of Michigan Elementary and Secondary School Growth Study. Along with the problems of bias due to its historic and

retrospective nature, it is not mentioned how the sample was selected and whether or not it was random.

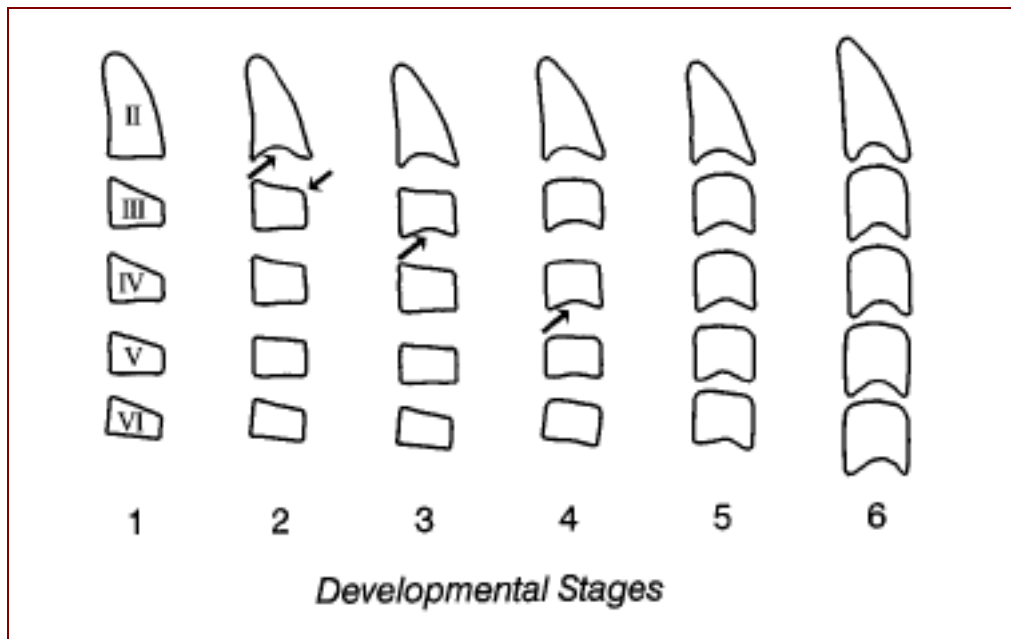


Figure 2.6: Six stages in cervical vertebral maturation (2000). Adapted from Franchi, Baccetti and McNamara (2000)²⁰

The main feature of the CVM method as described by Franchi, McNamara and Baccetti,²⁰ was the suggestion that the pubertal growth spurt (both statural height and mandibular growth) of almost 95% of North American patients coincided with the interval between Stage 3 and Stage 4 of the CVM Index.²⁰ They reported the predictability of this to be as high as 98.6%. They stated that if either Stage 1 or 2 CVM was recorded for patients then they had not yet had their growth spurt. This is a useful marker for identifying and predicting mandibular growth in patients with a class 2 malocclusion for whom treatment with a functional appliance is being considered.

Despite these advantages, there were some limitations to the CVM analysis. To make it easier to use and more applicable to the majority of patients, Franchi et al,²⁰ thought that these limitations must be addressed. Firstly, when a protective radiation collar was worn (more common at the time their work was first published), only the second, third and fourth cervical vertebrae were visible on the lateral cephalogram.¹⁶ Thus it was suggested that the CVM method should only use cervical vertebrae C2, C3, C4, as previously suggested by Hassel and Farman.¹⁹ Secondly, previous CVM staging had also included comparative assessments to help decide at which stage the CVM was but this required a series of radiographs. It was therefore suggested that the description of each stage should be worded so that the assessment could be made from a single cephalogram.¹⁶

Consequently, the same authors later introduced an improved version of the CVM staging method that only used the second, third and fourth vertebrae and included five maturational stages, instead of the six, in the former method.¹⁶ The five-stage CVM index is shown in Figure 2.7 and its descriptions in Table 2.1. The advantage of the new method was that the skeletal maturity could be appraised on a single cephalogram. In addition, because only the assessment of the second, third and fourth vertebrae were required, it means that lateral cephalograms taken for patients wearing a protective collar, could still be used. Again the sample used by Baccetti, Franchi and McNamara,¹⁶ was taken from the University of Michigan Elementary and Secondary School Growth Study, thus presented the same limitations as discussed previously.

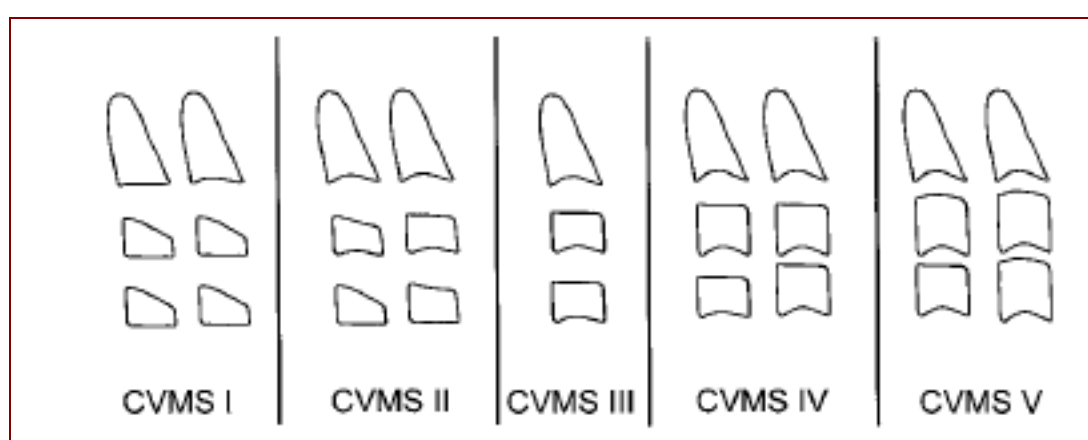


Figure 2.7: The newly improved CVM method (five developmental stages, CVMS I through CVM VI). Different combinations of morphological features in the bodies of C2, C3, and C4 are presented for the new method. Adapted from Baccetti, Franchi and McNamara.¹⁶

The improved CVM method is displayed in Figure 2.7. The descriptions for the five CVM stages were defined as detailed in Table 2.1.

CVM Stage	Definition
CVMS I	<p>The lower borders of all the three vertebrae are flat, with the possible exception of a concavity at the lower border of C2 in almost half of the cases.</p> <p>The bodies of both C3 and C4 are trapezoid in shape (the superior border of the vertebral body is tapered from posterior to anterior).</p> <p>The peak in mandibular growth will occur not earlier than one year after this stage.</p>
CVMS II	<p>Concavities at the lower borders of both C2 and C3 are present.</p> <p>The bodies of C3 and C4 may be either trapezoid or rectangular horizontal in shape.</p> <p>The peak in mandibular growth will occur within one year after this stage.</p>
CVMS III	<p>Concavities at the lower borders of C2, C3, and C4 now are present.</p> <p>The bodies of both C3 and C4 are rectangular horizontal in shape.</p> <p>The peak in mandibular growth has occurred within one or two years before this stage.</p>
CVMS IV	<p>The concavities at the lower borders of C2, C3, and C4 still are present.</p> <p>At least one of the bodies of C3 and C4 is squared in shape. If not squared, the body of the other cervical vertebra still is rectangular horizontal.</p> <p>The peak in mandibular growth has occurred not later than one year before this stage.</p>
CVMS V	<p>The concavities at the lower borders of C2, C3, and C4 still are evident.</p> <p>At least one of the bodies of C3 and C4 is rectangular vertical in shape. If not rectangular vertical, the body of the other cervical vertebra is squared.</p> <p>The peak in mandibular growth has occurred not later than two years before this stage.</p>

Table 2.1: Definitions of new improved CVM stages. Adapted from Baccetti, Franchi and McNamara.¹⁶

Further to this, the same authors again reworked the CVM Index in 2005, reverting back to a six stage index, which is shown in Figure 2.8.¹⁵ They stated this revised version was a more valid and a more practical staging method to apply. Stage 1 and 2 were classified as pre-peak stages, with the mandibular growth peak occurring between stage 3 and stage 4. Stage

6 described a stage that indicated that the peak in growth had occurred at least two years earlier.

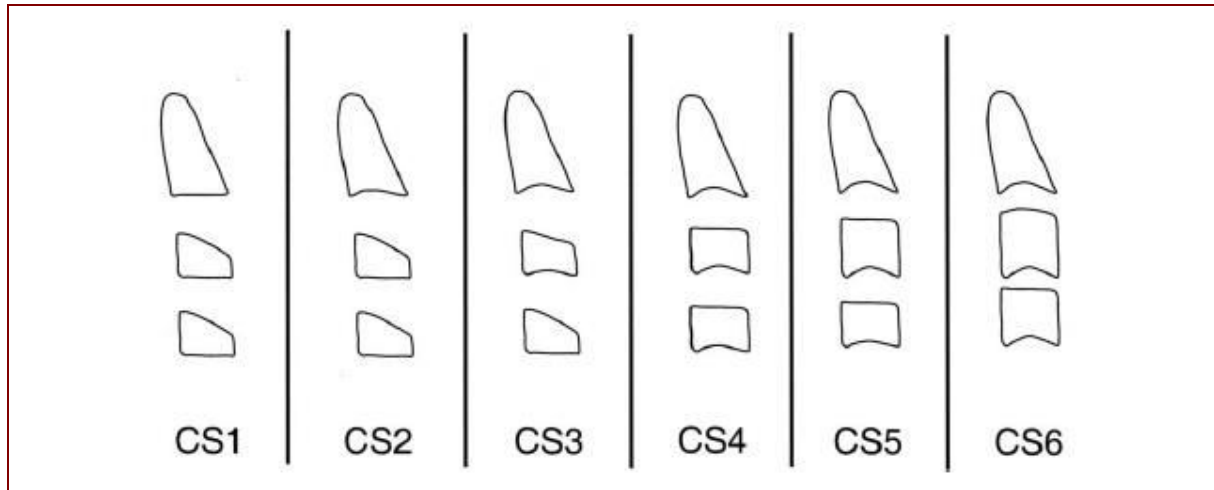


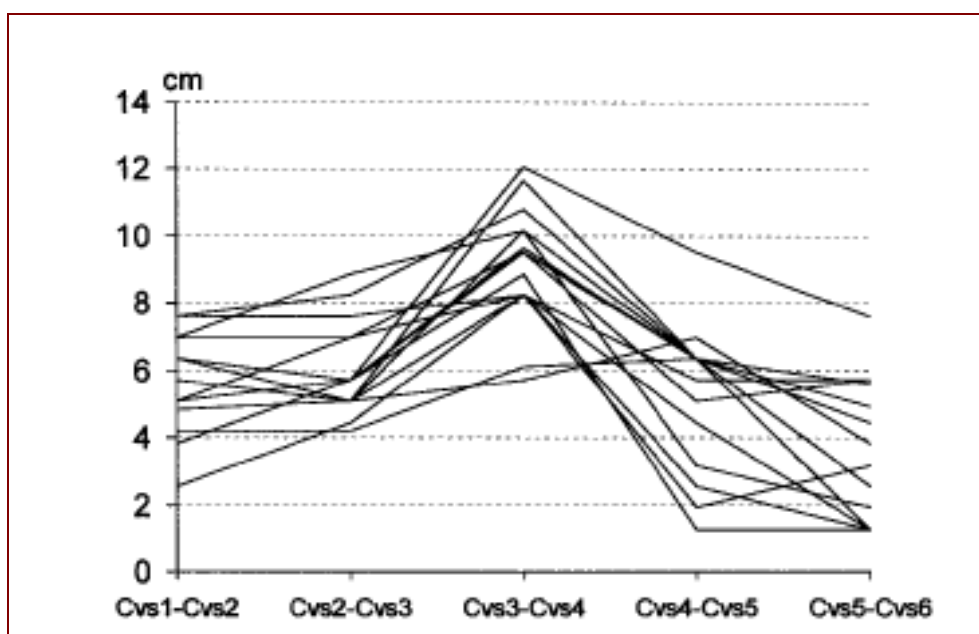
Figure 2.8: Schematic representation of the stages of cervical vertebrae according to the newly modified method. Adapted from Baccetti 2006.¹⁵

2.4.4: Relationship of CVM to mandibular growth

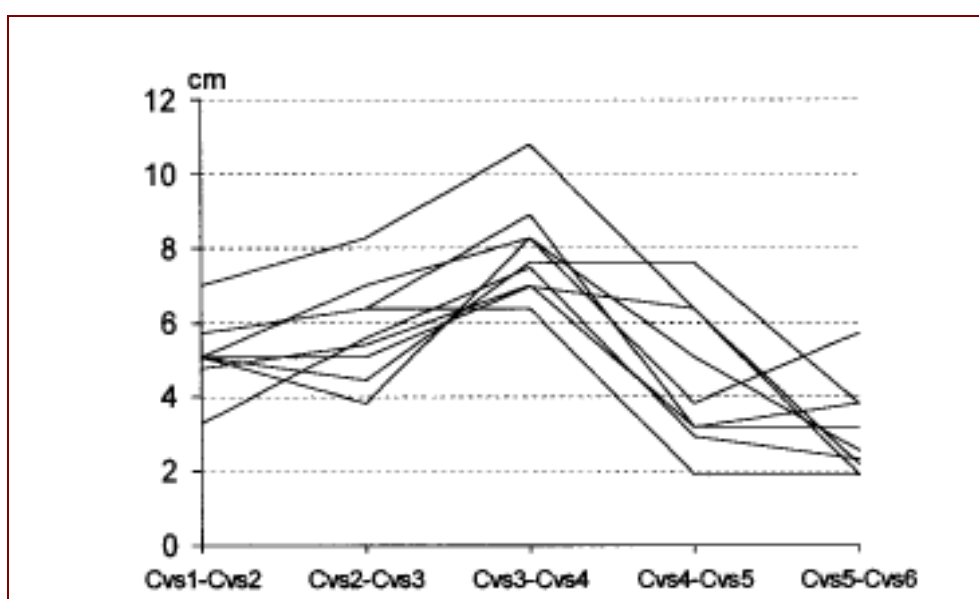
O'Reilly and Yanniello¹⁸ initially assessed the relationship of the CVM stage to mandibular growth using an historic sample, for 13 subjects, taken from the Bolton-Broadbent growth study.¹⁸ They reported that there was a positive association between cervical vertebral maturation and mandibular growth changes during puberty. Franchi²⁰ corroborated these findings in their 2000 study in which they demonstrated that peak mandibular growth occurred between Stages 3 and 4 of the modernised CVM index. However, the sample size in this study was only 24 so the results must be interpreted with caution.

2.4.5: Relationship of CVM to Standing Height

Franchi et al,²⁰ also reported that the peak velocity of change in statural height occurred between CVM stages 3 and 4, thereby linking the CVM stage to changes in statural height.²⁰ They found that 100% of boys and 87% of girls had their peak in growth velocity at this interval; this can be seen clearly in Figure 2.9.²⁰ The findings demonstrated in the graphs in Figure 2.9 show that peak increases in statural height and mandibular length both occurred between stage 3 and stage 4.²⁰



A: Females n=15



B: Males n=9

Figure 2.9: Individual changes in stature height at intervals between stages in cervical vertebral maturation. A: a subgroup of 15 females B: a subgroup of 9 males. Adapted from Franchi, Baccetti and McNamara.²⁰

2.4.6: Relationship of standing height to dentofacial growth

There is scarce but strong evidence showing an association between standing height and dentofacial growth. Mitani and Sato made a good attempt when they explored a possible relationship of mandibular growth compared to numerous clinical variables including

standing height.⁷³ However, they concluded that there was a large range of variability between the different variables and that mandibular growth showed the most variation, thus this association remains inconclusive.⁷³

2.4.7: Reliability of Cervical Vertebral Maturation Staging

Any diagnostic tool must be both valid and reliable, yielding reproducible results in a consistent manner, measuring what it reports to measure with minimal inter- and intra-operator variation.^{81, 93, 94} The reliability of the CVM Index has been reported by many authors, with a range of results from perfect agreement to extremely poor agreement.^{41, 79, 95, 96} However, many of the studies have significant limitations that make it difficult to draw any solid conclusions. These include the sample size of the observers and/or images, the use of traced vertebral images rather than assessment using the radiographic image together with the use of observers who had increased knowledge and training of the CVM method or who were involved in its development. A systematic review, published by Santiago et al, highlighted these issues and suggested a more accurate method of testing reliability to determine whether the CVM index was a clinically applicable tool.⁹⁷ To meet many of these limitations, Rainey in an unpublished thesis²⁷ carried out a reliability study involving a group of 20 orthodontic clinicians, with a range of experience, and no previous training or experience in the CVM staging method. She assessed the reliability of staging 72 consecutive lateral cephalograms over 2 phases. She reported an overall 89% intra-observer agreement and 88% inter-observer agreement; concluding that the CVM staging method was reproducible and reliable.

2.4.8: Validity of cervical vertebral maturation index

Many authors have also discussed the validity of the CVM staging method. Mitani and Sato demonstrated a correlation between changes in the cervical vertebrae and mandibular size.⁷³ Several authors have found a significant correlation between CVM and skeletal maturation of the hand-wrist bones.^{16, 19, 39} Finally, Baccetti and Franchi demonstrated the validity of this method with regards to predicting the pubertal peak and evaluating skeletal maturity in their work, also using hand-wrist radiographs as a reference.^{15, 16, 20} However, Engel et al.⁹⁸ have recently suggested that the CVM staging method could not predict craniofacial growth in girls with a class 2 malocclusion, but this study was based on a sample of girls from the Nijmegen growth study, which was published in 1979 and thus comprised of a historic sample, thus its relevance and generalisability to today's children is questionable.

It would seem therefore, that cervical vertebral staging is probably a valid method of assessing skeletal maturity. The appeal of this index to orthodontists, if proved to be valid on

an appropriate sample, is that it uses information that is readily available to us on a lateral cephalogram, which is taken routinely for orthodontic diagnosis and thus does not require any additional radiation exposure. However, to date, all the studies that have assessed the validity of CVM staging have used historic samples and have been conducted in a retrospective manner. The validity has not yet been prospectively investigated using a contemporaneous sample.

2.4.9: Summary of Main Growth studies

There are a number of longitudinal growth studies, most of which were undertaken in the United States roughly between 1930 and 1985.⁹² Collections of radiographic images (both lateral cephalograms and hand-wrist radiographs) and other records of craniofacial development of growing children with malocclusions who did not receive orthodontic treatment have been archived at various Universities in North America.

Prior to 1930, the cephalostat was not in use and thus standardized imaging of the craniofacial region was not routinely being undertaken. Towards the late 1900s the harmful effects of ionizing radiation had been recognised and legislation was starting to come into effect about the exposure of patients to ionising radiation. Thus, longitudinal studies of this nature are unlikely to be repeated. The information from these longitudinal studies has been of significant value to the orthodontic profession with regards to studying the natural course of growth of the subjects in the growth studies. The main growth studies are summarised in the table below (Table 2.2).

These growth studies have been used as a sample or control group for many of the CVM reliability and validity studies.⁹² However, it is recognised that populations change with time, and what may have applied to a historic sample, may no longer be valid.⁹³ This is a common issue for studies that have used samples from historic growth studies. Although these studies have contributed to our knowledge of growth and development, the findings of studies that use samples from historic growth studies must be interpreted with caution due to their limitations.

<u>Name of Study</u>	<u>Institution</u>	<u>Date</u>	<u>Original Author and Curator</u>	<u>Number of subjects</u>	<u>Details</u>	<u>Records</u>
The Case Western Bolton Brush Growth Study	Bolton Brush Growth Study Centre, Case Western University	1930-1977	B. Holly Broadbent Sr. (Bolton Family) (Curator Mark G Hans)	4309	Houses largest human craniofacial growth study in world: Broadbent-Bolton Growth study and largest longitudinal growth study: the Brush Inquiry	Radiographs (lateral cephalograms, hand wrist radiographs) Study Models (SMs)
The University of Toronto Burlington Growth Study	Department of Orthodontics, Dental School, The Burlington Growth Centre University of Toronto	1952-	Dr. Robert Moyers Curator Bryan D Tompson	1258	The predominant racial group was Caucasian & mostly Anglo Saxon. To date, there have been 339 studies using the Burlington Growth Centre information.	Cephalometric radiographs, hand-wrist radiographs, SMs Height and weight; photographs
The University of Oklahoma Denver Growth Study	Department of Orthodontics - Dental School, University of Oklahoma	1927-1967	Curator G. Fräns Currier	313	Untreated children, European Caucasians	Lateral Cephalograms Handwrist radiographs Facial photographs Study Models Full body photographs

<u>Name of Study</u>	<u>Institution</u>	<u>Date</u>	<u>Original Author and Curator</u>	<u>Number of subjects</u>	<u>Details</u>	<u>Records</u>
The Wright State University Fels Longitudinal Study	Lifespan Health Research Center - Wright State University	1929-1982 (cranial radiographs terminated)	Curator Richard Sherwood	1200	Largest and longest running study of human growth over the lifespan (Roche, 1992). Study participants live in or near southwest Ohio (Indiana, Kentucky, West Virginia) and were born between 1929 and present.	Lateral Cephalograms Handwrist radiographs Knee radiographs
The Forsyth Institute Twin Sample	Forsyth Institute		Dr. Coenraad Moorrees Curator Ahmet Keles	533 families with twins or triplets recruited	The Forsyth twin sample is perhaps the largest prospective growth sample collected on twins and their families. The sample was collected as part of a federally funded project carried out at the Forsyth Infirmary for Children in Boston, Massachusetts	Lateral (open and closed mouth) and posteroanterior cephalograms, incisor periapicals during incisor eruption, hand-wrist films, SMS.
The Iowa Facial Growth Study	Department of Orthodontics - College of Dentistry, University of Iowa	1946-1968	Howard V. Meredith and L. B. Higley Curator Thomas E. Southard	183	Although the study is called "Facial Growth," numerous trunk and limb measurements also measured. Height, weight, dietary information, and medical history data included.	SMS, anterior and profile photographs, and full intraoral radiographs, PA and lateral cephalometric radiographs

<u>Name of Study</u>	<u>Institution</u>	<u>Date</u>	<u>Original Author and Curator</u>	<u>Number of subjects</u>	<u>Details</u>	<u>Records</u>
The UOP Mathews Growth Study	Collected at University of California at San Francisco	1967-1979	Dr. J. Rodney Mathews Curator Sheldon Baumrind	36	The Mathews Implant Growth Study collection is uniquely important because it is the only longitudinal cephalometric record set from subjects with Björk type implants.	Lateral, PA, and oblique cephalograms
The Michigan Growth Study	Department of Orthodontics and Pediatric Dentistry, Ann Arbor Campur, University of Michigan	1935-1970	Curator James A. McNamara	721 individuals 150 families	Subjects primarily Northern European ancestry. Bias toward Class II malocclusion and increased lower anterior facial height, with only a very few individuals presenting with Class III malocclusion.	Lateral cephalogram closed, lateral cephalogram open, posteroanterior, lateral obliques (2), and hand/wrist films.
The Oregon Growth Study	Department of Orthodontics - School of Dentistry, Oregon Health and Science University	1950-1975	Curator David A. Covell Jr.	357	The records were collected from untreated Caucasian individuals, either semiannually or annually	Photographs, SMs, lateral (closed and open), P-A, hand-wrist and intraoral films, growth charts, diet records, and health-histories.

Table 2.2: A summary of the main growth studies; Adapted from American Association of Orthodontists Foundation: Craniofacial Growth Legacy Collection⁹²

2.5: Readability of Information

Evidence suggests that patients overall satisfaction with a clinician is increased if they are given and understand, information and advice provided.¹⁰⁰ It has been shown that patients forget or misunderstand much of what is discussed during a consultation.¹⁰¹ It has been reported that patients will retain 20% of what is discussed but this will increase up to 50% if there is additional visual or written input.¹⁰² George et. al.¹⁰³ demonstrated that patients favoured written information and that patients who were given leaflets were more satisfied with their treatment as a whole.

Although participating in the current study did not involve any treatment for the participants and merely involved participants having their height measured, it was anticipated that patients and parents would be happier if they were provided with adequate information about the study that was communicated at the appropriate level. Weinman¹⁰⁴ confirmed the desire, use and value of leaflets by patients, showing that 75% of patients wanted written information and that 80% read the leaflets.

Readability formulae assess the structural elements of text and are designed to measure the reading difficulty or the ease with which written text can be understood by a reader.¹⁰⁵ The readability of a particular text depends on both its content (for example the complexity of its vocabulary) and on its typography (for example its font size, line height and line length). There are over 50 published readability formulae that produce a score or number that indicates to what extent a piece of text is readable.¹⁰⁰ Most are based on the theory that longer words and sentences are harder to understand.¹⁰⁵

Reading abilities vary widely across a population and across different age groups so it is important that information is pitched at a suitable level for it to be understood by the target audience.¹⁰⁶ It is a common finding that patient information leaflets (PILs) tend to be written at too high a level for the target audience. Harwood and Harrison¹⁰⁵ looked at 26 orthodontic PILs from professional organisations and commercial companies and found that the mean readability of all the PILs was rated as 'fairly difficult', meaning that only 40% of the UK population would be expected to understand them.

2.5.1: Flesch-Kincaid Reading Ease

In the Flesch Reading Ease test, higher scores indicate material that is easier to read; lower numbers indicate that the text is more difficult to read.¹⁰⁷

Rudolf Flesch published his Reading Ease formula in two parts in 1948.¹⁰⁷ Rather than using grade levels, it used a scale from 0 to 100, with 0 equivalent to the 12th grade (USA) and 100 equivalent to the 4th grade (USA). The second part of the formula predicts human interest by using personal references and the number of personal sentences. The original formula is:

$$\text{Reading Ease score} = 206.835 - (1.015 \times \text{ASL}) - (84.6 \times \text{ASW})$$

Where: ASL = average sentence length
 = $\frac{\text{Number of words}}{\text{Number of sentences}}$

ASW = average word length in syllables
 = $\frac{\text{Number of syllables}}{\text{Number of words}}$

The Flesch Reading Ease formula became one of the most widely used, and the one most tested and reliable. In 1951, Farr, Jenkins and Patterson simplified the formula further by changing the syllable count¹⁰⁸. The modified formula is:

$$\text{Reading Ease score} = 1.599\text{NOSW} - 1.015\text{SL} - 31.517$$

Where: NOSW= number of one-syllable words per 100 words and

SL= average sentence length in words

2.5.2: Flesch–Kincaid Grade Level

In 1975, in a project sponsored by the U.S. Navy, the Reading Ease formula was recalculated to give a grade-level score. This new formula uses the "Flesch–Kincaid Grade Level Formula" to translate the 0–100 score to a school grade level, facilitating the categorisation of readability level of texts.¹⁰⁷ The result is a number that corresponds with a grade level. For example, a score of 8.2 would indicate that the text is expected to be understandable by an average student in year 8 (aged 12-13 years) in the United Kingdom. The Flesch-Kincaid formula is one of the most popular and heavily tested formulas.

2.5.3: Gunning Fog Index

This index estimates the years of formal education needed to understand the text on a first reading.¹⁰⁹ Robert Gunning developed this index in the 1940s whilst he was running a readability consulting firm which was dedicated to reducing the 'fog' in newspapers. In 1952, he published the Gunning-Fog Index,¹⁰⁹ a formula that is reliable and simple to apply:

$$\text{Grade level} = 0.4 \times [(\text{average sentence length}) + (\text{percentage of Hard Words})]$$

Where: Hard words = words with more than 2 syllables.

A Fog index of 12 requires the reading level an 18 year-old. Texts for a wide audience generally need a Fog index of less than 12. Texts requiring almost universal understanding need a Fog index of less than 8.

2.5.4: SMOG

The SMOG grade is another measure of readability.¹¹⁰ It was published by McLaughlin in 1969, and he determined that word length and sentence length should be multiplied rather than added as in other formulae. The SMOG formula is:

SMOG grading = 3 + square root of polysyllable count

Where: polysyllable count = number of words more than two syllables in a sample of 30 sentences.

The SMOG grade is thought to be more accurate and more easily calculated than the Gunning-Fog index and recently it was concluded that the SMOG grade was the gold standard formula for consumer-orientated healthcare materials with regards to readability formulae.¹¹¹

2.5.5: Automated Readability Index

The Automated Readability Index (ARI) is a readability test that produces an approximate representation of the US grade level needed to comprehend the text.¹¹² The formula for calculating the ARI is:

$$\text{ARI} = 4.71 (\text{characters} / \text{words}) + 0.5 (\text{words} / \text{sentences}) - 21.43$$

Where: characters: is the number of letters, numbers and punctuation marks

Words: is the number of spaces

Sentences: is the number of sentences

US grade level 1 corresponds approximately to ages 6 to 8. Reading level grade 8 corresponds to the typical reading level of a 14 year-old child.

In order for the information material to be readable to the majority of our participants and their parents, information about the study was written in a simple form and assessed using the above criteria prior to ethical approval being granted.

2.6: Measuring Mandibular Growth

There was much discussion on how the velocity of mandibular growth should be assessed. Mandibular growth occurs as the result of a heterogeneous pattern of bone resorption and apposition.¹¹³ Our current knowledge of the extent to which the mandible changes and

rotates during growth mostly derives from classical longitudinal studies that were based on serial two-dimensional cephalometric radiographs superimposed on bone markers.¹¹⁴ This approach, however, has questionable accuracy, is prone to measurement error, and the information obtained is limited by the two-dimensional nature of the image.¹¹⁵ The introduction of three-dimensional radiographic imaging with cone-beam computed tomography (CBCT) now allows quantitative and qualitative analysis of bone remodelling that could potentially allow the original concepts of growth to be reassessed. However, ethically for the purposes of this study, this type of radiographic imaging, for the purpose of determining the velocity of mandibular growth, was not appropriate.

This led to a quandary as to how the velocity of mandibular growth should be determined. It was thought that looking to previous research to see what previous authors had done would allow the use of a method that was comparable to other research done on this topic. Franchi et al²⁰ used two triangles as shown in Figure 2.10; Co-Gn-Go and S-Gn-Go. There are advantages associated with each of these triangles. Using sella as a reference point to gnathion and gonion provides a stable reference from which forward anterior-posterior and vertical growth can be assessed. However, using condylion would provide possibly a more accurate measure of mandibular growth, as it would take into account growth or remodelling that had occurred at the condyle. This would hopefully mean that growth in any direction would be taken into account when measuring the area of the triangle Co-Gn-Go.

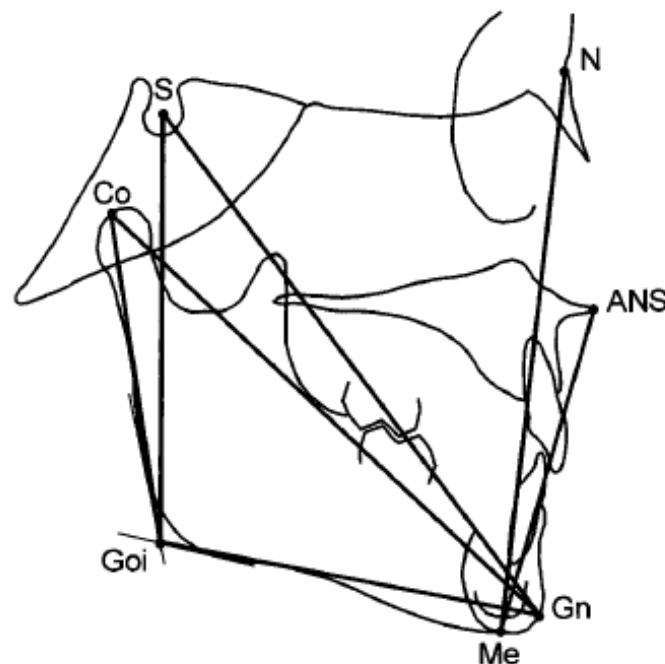


Figure 2.10: Measurements used to assess mandibular growth in the Franchi et al 2002 paper. Modified from Franchi et al.²⁰

Several other methods of assessing mandibular growth have been described in recent research. O'Brien et al¹¹⁶ used Pg/Olp and Co/OLp from the Pancherz analysis to assess skeletal changes that had occurred after the use of functional appliances. However, in his discussion of randomised clinical trials on treatment of class II malocclusions, Miele reports that the analysis of Pancherz (1982), underestimates mandibular growth, as it is a linear measurement that does not take into account individual variation in condylar growth rotation.¹¹⁷

Others methods of measuring mandibular growth that have been described in the literature include using Co-Pg^{118,119} and Co-Gn¹²⁰ to describe mandibular changes. Mitani and Sato⁷³ looked only at condylion-gonion to assess mandibular growth, with the idea that this would take into account both vertical and antero-posterior mandibular growth that had occurred. This, however, may result in any growth or remodelling at the angle of the mandible being missed.

Hunter,¹³ when assessing mandibular growth in relation to standing height and skeletal maturation, used 7 linear measurements; Ar¹-Go⁶, Go⁶-Po⁵, Ar¹-A⁴, S²-N³, S²-Go⁶, N³-M, shown in Figure 2.11. Bishara et al. also used articulare, but instead used articulare-pogonion to assess mandibular length.¹²¹ Articulare has high reproducibility, however, it does not show full mandibular length. Articulare will not undergo the same positional change following a change in the amount or direction of growth in the mandible. In addition, measuring mandibular length with articulare introduces the possibility of a false interpretation of an increase in mandibular length, if the condyles are positioned anteriorly within the glenoid fossa,

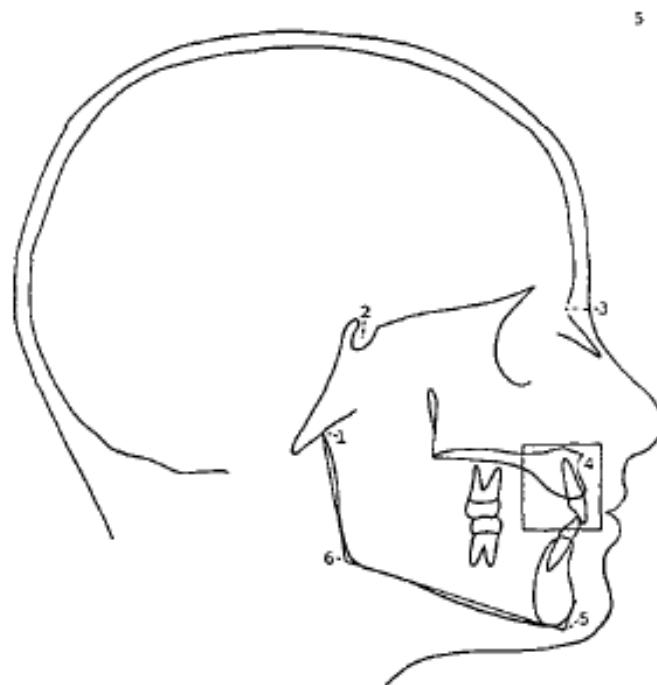


Figure 2.11: Measurements used to assess mandibular growth in Hunter (1966). Modified from Hunter.¹³

As the research carried out by Franchi et al.²⁰ was most similar to this study, with similar outcome variables, it was thought that it was most appropriate to have comparable data to their research. To avoid an excess of spurious data, it was decided that the triangle Co-Gn-Go to assess mandibular growth should be used.

One of the problems with using this assessment was the difficulty in defining the head of the condyle (condylion) on a lateral cephalogram. Condylion is well documented to have a high degree of error in its identification.¹²² Adenwalla suggested that if the mandibular condyle has to be used as a landmark in a study, that an open mouth cephalogram should be taken and superimposed on the respective cephalogram in normal occlusion, to obtain the most accurate and reliable measurements.¹²³ However, there is conflicting evidence in the literature as to whether an open mouth cephalogram does indeed improve the accuracy and reliability of the identification of condylion.^{123, 124} In addition, for the purposes of this research, as cephalograms that had already been taken for orthodontic treatment planning in the closed mouth position, were being used, the open mouth method was not an option.

Furthermore, Meikle has suggested that the linear dimension condylion-gnathion will be strongly influenced by condylar growth rotations.¹¹⁷ In using cephalometric radiographs to assess mandibular growth, it is almost impossible to identify and accurately measure mandibular growth rotations. It has been shown that longitudinal growth of the mandible is

confined to the condyle and the direction of condylar growth is highly variable,^{12, 125} thus highlighting the importance of considering growth rotations when assessing mandibular growth. The limitations of cephalometrics must be taken into account, and cephalometric data critically assessed.

Chapter 3: Rationale for Research

The importance of determining a patient's growth stage has been clearly described^{1, 20} and the CVM index provides a tool that is easy to apply, readily available to orthodontists and has been shown to be reliable.²⁷ Previous research carried out on the CVM method has focussed on its inter- and intra-observer agreement^{27,126} and on determining the correlation between the CVM index and the hand-wrist radiograph index.^{16, 19, 39}

However, research validating CVM with regards to the prediction of growth, both standing height growth and mandibular growth is sparse. Despite the index having been shown to be valid,^{16, 20, 52} the existing research has been retrospective and has used historic samples from growth studies carried out in the US started in the early 1900s.

For the CVM method to be of use clinically today, it must not only be reliable but it must also be valid with respect to its predictability of growth in a contemporary sample. The aim of this study is therefore to determine the validity of the cervical vertebral maturation as a predictor for growth using an appropriately sized contemporaneous sample in a prospective manner.

Chapter 4: Lateral Cephalogram Audit

There are many benefits of applying the Cervical Vertebral Maturation (CVM) staging method to assess the stage of growth and development at which orthodontic patients have reached. The use of this method can allow the orthodontist to make much more informed decisions regarding the timing of treatment and treatment modalities. The CVM staging method has been shown to be reliable.²⁷ However, in order to use this method, the second, third and fourth cervical vertebrae need to be visible on the lateral cephalogram.

4.1: Aim

The aim of this audit was, therefore to evaluate whether lateral cephalograms, taken at Liverpool University Dental Hospital, routinely included the second, third and fourth cervical vertebrae, allowing application of the Cervical Vertebrae Maturation (CVM) staging index (Figure 4.1).

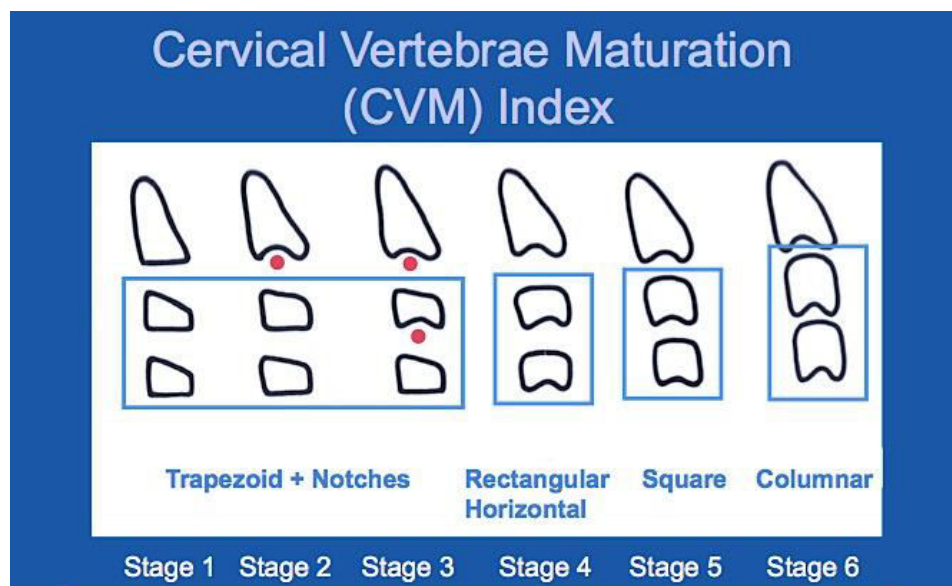


Figure 4.1: CVM Index taken from Baccetti et al.¹⁵

4.2: Standards

All lateral cephalograms should include the second, third and fourth cervical vertebrae³ and the cervical vertebrae image should be of a sufficient diagnostic quality.

The standard was therefore set that 90% of lateral cephalograms would have a clear representation of the second to fourth cervical bodies.

4.3: Design and Setting

This was the third phase of an on-going audit looking at lateral cephalograms from three consecutive first year Specialty Registrar (StR) patient cohorts at Liverpool University Dental Hospital. The audit was registered with the clinical effectiveness unit.

In the first audit, undertaken by B-J Rainey, all lateral cephalograms requested by first year orthodontic registrars from the 1st October 2010 to 31st January 2011, were assessed retrospectively for the inclusion of the second, third and fourth cervical vertebrae and the ability to stage the CVM (Figure 4.2). The target was not met and failure to attain the target appeared to be a result of the patient being positioned incorrectly in the cephalostat, with the patient's neck often appearing hyperextended.

As a result of this, staff in the radiology department were provided with appropriate training on positioning patients correctly in natural head posture when having a lateral cephalogram taken. After a washout period, the second cycle was carried out to assess if there had been an improvement.

The second stage of the audit, also undertaken by B-J Rainey, looked at lateral cephalograms taken from October 2011 to January 2012.

This third phase hoped to complete the audit cycle and looked at a randomly selected group of 80 lateral cephalograms taken between October 2012 and January 2014.

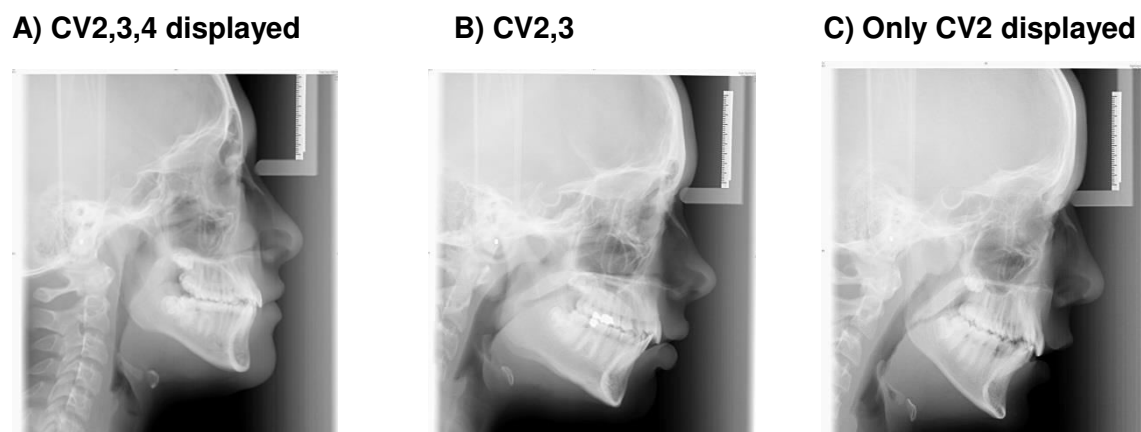


Figure 4.2: Assessment Criteria: Lateral cephalogram clearly displaying: A) CV2, CV3 and CV4, B) CV2 and CV3, C) Only CV2

4.4: Results

First audit October 2010-January 2011

In the first audit cycle undertaken by B-J Rainey, a total of 264 lateral cephalograms were assessed. Of these radiographs, 100% of them displayed CV2, 97% clearly displayed CV3,

however, only 83% of the lateral cephalograms clearly displayed CV4. Thus, only 83% of the radiographs were suitable for the application of the CVM method described by Baccetti.³⁸ (Table 4.1).

In the first audit the target, of 90% of lateral cephalograms having CV2, 3 and 4 displayed, was therefore not achieved.

Second Audit October 2011- January 2012

In the second cycle (B-JR), 134 lateral cephalograms were assessed. Again, all lateral cephalograms in this sample clearly displayed CV2. The percentage clearly displaying CV3 increased to 100% and the percentage clearly displaying CV4 increased to 93%. Therefore, CVM staging could be applied in 93% of cephalograms assessed (Table 4.1).

Overall, the ability to stage lateral cephalograms using the Baccetti¹⁵ method of CVM staging improved from 83%, in the initial audit, to 93% in the re-audit. This improvement was statistically significant [OR 2.72 (1.08, 6.89)].

Third Audit October 2012- January 2014

In the third cycle, undertaken by SH, 80 cephalograms were assessed according to the same criteria. All the lateral cephalograms displayed CV2. The percentage displaying CV3 was 96% and 85% displayed CV4. Therefore CVM staging was possible in 85% of cephalograms assessed.

Overall, from the second phase to the latest (third phase) re-audit, the ability to stage lateral cephalograms using the Baccetti method of CVM fell from 93% in the first to 85% in the final audit cycle. Nevertheless, this change was not statistically significant [OR 0.41 (0.16-1.02)] but the target of 90% of cephalograms having CVM 2, 3,4 visible was again, not met.

	Number. of Cephs	Number with C2	% with C2	Number with C3	% with C3	Number with C4	% with C4	Number with CVM2,3,4	% All with CVM2,3,4
FIRST AUDIT OCT 2010-JAN 2011 (BJR)	264	264	100%	256	97%	219	83%	219	83%
SECOND AUDIT OCT 2011-JAN 2012 (BJR)	134	134	100%	134	100%	125	93%	125	93%
THIRD AUDIT OCT 2012-JAN 2014 (SH)	80	80	100%	77	96%	68	85%	68	85%

Table 4.1: Results from first audit (October 2010-January 2011), second audit (October 2011- January 2012) and third audit cycle (October 2012-January 2014).

4.5: Discussion

The first audit found that 17% of the lateral cephalograms were not suitable for application of the CVM method. This was similar to a clinical trial that reported that it was not possible to stage 16% of lateral cephalograms using the Hassel and Farman method as the radiographs were not clear in the cervical vertebrae region.¹²⁷

The results of the audits undertaken at Liverpool University Dental Hospital show that CV2 was present on all cephalograms and it was CV3 and/or CV4 that were not visible. It was identified that this was a result of patient positioning because when patients were positioned with their neck hyperextended, rather than in a more vertical position, and not in natural head position, the cervical bodies of CV4 and CV3 may be cropped from the radiographic field. Poor patient positioning has been confirmed in the literature as a significant factor in the accuracy of determining the CVM Stage.¹²⁸ Torres et al. showed that upward or downward head inclination adversely affected the ability to evaluate the CVM stage and that inter-observer agreement was higher in the lateral cephalograms taken in natural head position.¹²⁸

In the third audit cycle, although it appears that the number of radiographs to which the CVM method can be applied has fallen again, the sample size was significantly lower and so even though randomly chosen, may not have been representative.

Another potential reason for this variation is the nature of Liverpool University Dental Hospital (LUDH) as a teaching hospital whereby a number of trainee radiographers pass through the department, meaning that the radiographers who received the training in 2011, may not have been those who were taking the radiographs in the most recent audit. This will be a general problem encountered in all teaching hospitals and thus it may be helpful to include this information about patient positioning in the cephalostat as an on-going educational programme, when training new radiographers to take lateral cephalograms.

4.6: Conclusion

The target, that 90% of lateral cephalograms had the second, third and fourth cervical vertebrae clearly visible, was met in the second cycle but was not met in the first and third cycles. Providing training to the radiographers who were taking the lateral cephalograms significantly increased the number of lateral cephalograms that displayed the second, third and fourth vertebrae, thus allowing the 90% standard to be achieved in the second audit. However, this was not maintained in the long term and measures need to be taken to ensure the ongoing training of radiographers in the radiology department at LUDH.

4.7: Recommendations

Failing to display the second, third and fourth cervical vertebrae clearly on a lateral cephalogram is usually a result of incorrect patient positioning in the cephalostat. Discussions have been held with the consultant radiologist at LUDH in an attempt to determine the best way of ensuring that the radiographers position patients correctly in the cephalostat. Agreement was obtained to place a poster close to the cephalostats illustrating the ideal head position to ensure that CVM 2,3,4 are included on the lateral cephalogram, Following this, J.Mangan, orthodontic StR will re-audit the lateral cephalograms taken following the instigation of any training package and use of an 'aide memoir'.

Chapter 5: Study Objectives

5.1: Primary Study Objective

To assess if a correlation exists between CVM Stage and statural height growth velocity.

5.2: Secondary Study Objectives

To assess if a correlation exists between:

1. CVM Stage and mandibular growth velocity.
2. Mandibular and statural height growth velocities.

Chapter 6: Null Hypothesis

6.1: Null hypotheses

There is no correlation between CVM Stage and statural height growth velocity against the alternative hypothesis of a correlation.

There is no correlation between CVM Stage and mandibular growth velocity against the alternative hypothesis of a correlation.

There is no correlation between mandibular and statural height growth velocities against the alternative hypothesis of a correlation.

Chapter 7: Methods and Participants

7.1 Design

This was a prospective, longitudinal observational cohort study investigating the correlation between cervical vertebral maturation, statural height and mandibular length of treated orthodontic patients.

7.2 Method

Participants were recruited into the study during the early stages of their orthodontic treatment. Routine orthodontic clinical records were collected from all patients as per the departmental protocol and used for treatment planning (see Figure 7.1). These records included taking the patients' initial standing height and obtaining a lateral cephalogram radiograph. Following this, patients started orthodontic treatment, as appropriate, to correct their malocclusion.

Routine care was provided as per the consultants' treatment plan. Interim and final records were obtained as clinically necessary.

In addition to this routinely acquired information, it was planned that the operator would take a measurement of standing height at each visit and record it in the clinical records.

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7.1 Table of Study Steps and Data Collection

Study Steps	Start records	Treatment planning	Each treatment appointment	Post functional treatment	Pre finish records	Post debond records
Patient information and informed consent	X	X				
Study models	X	X		X	X	X
Extra-oral photographs	X	X		X		X
Intra-oral photographs	X	X	X	X	X	X
Lateral Cephalogram (as clinically required)	X			X	X	
Dental panoramic tomograph (as clinically required)	X					
Intra-oral radiographs (as clinically required)	X					
Standing height*	X	X	X	X	X	X

*Standing height was measured with the patient barefoot, and in natural head position (Frankfort plane parallel with the ground) at every visit and in conjunction with national guidelines.⁶⁹

Table 7.1: Table of Study Steps

7.4 Sample

7.4.1 Participant Selection

All participants were contacted to start orthodontic treatment having been on the waiting list at Liverpool University Dental Hospital and having been assessed as being suitable for treatment under the NHS criteria for care. At their first appointment, routine history, examination and special investigations were undertaken after which the patient and their parent/guardian were informed about the study and invited to participate. All patients underwent standard assessment, orthodontic diagnosis and treatment planning.

At their second appointment, the patients' treatment plan was discussed and consent to participate in the study was obtained from willing participants and their parents/guardians.

7.4.2 Inclusion criteria

Participants were included if they:

- Were between the ages of 8-18 years,
- Were of either gender, male or female
- Had not had previous orthodontic treatment,
- Had commenced treatment with first year StRs in the academic year 2012-2013,
- They and their parent/guardian had given informed consent/assent to participate in the study.

7.4.3 Exclusion criteria

Participants were excluded if they:

- Were over the 18 years of age threshold at the start treatment "records" appointment.
- Had previously received orthodontic treatment.
- Had been diagnosed with any congenital clefts of the lip or palate, or known or suspected craniofacial syndromes or growth related conditions.
- Did not consent to take part in the study.

7.4.4 Measurements used

7.4.4.1: Standing height

It was planned that standing height would be measured in barefoot, with the patient in natural head position (Frankfort plane parallel with the ground) at every visit and in conjunction with national guidelines,⁶⁹ and recorded and stored in the patients' notes. It was measured using a wall mounted stadiometer.

Taking the standing height at each visit (every 6-weeks) was the only intervention that was in addition to routine clinical practice. It took approximately 5 minutes at the start of each appointment. It was carried out by the treating StR in a designated area, on route between the waiting room and the clinic. The height was recorded on a data sheet in the patients' notes.

7.4.4.2: Cephalometric measurements

Lateral cephalograms (which include the cervical vertebrae) were taken:

1. At the start of treatment,
2. On completion of post functional appliance therapy (if undertaken)
3. Prior to debond and completion of active intervention (as required).

Lateral cephalograms were traced and analysed by hand. A random 10% sample was retraced to assess the method error and reproducibility. To ensure the data were comparable with previous research, the following cephalometric variables were included (Figure 7.2):

- Measurements of mandibular size (Co-Gn, Co-Go, Go-Gn).

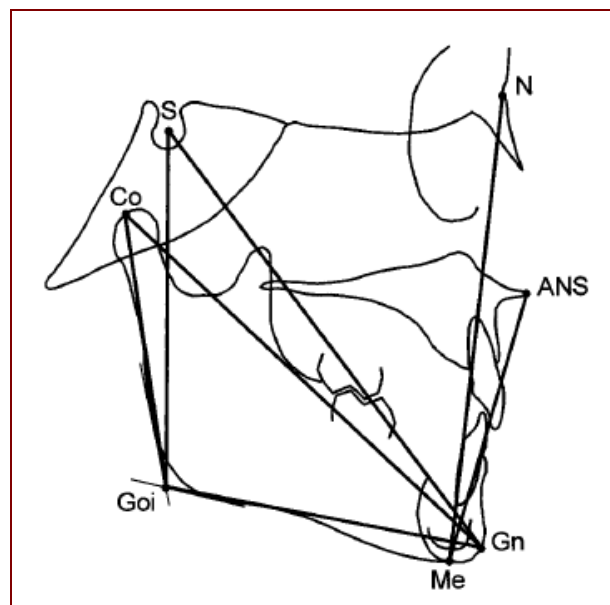


Figure 7.2 – Cephalometric landmarks and measurements. Adapted from Franchi et al.²⁰

7.4.5 Consent

Originally, one participant information leaflet and one participant consent form were designed for the study; however, the child assent form was produced after attending the research ethics meeting to obtain ethical approval for the study.

The local research ethics committee commented that the participant information leaflet (PIL) and consent form may be too difficult for 8-12 year olds to comprehend. In response to this, a new combined information and assent form was written for the younger participants using simple language and pictures demonstrating the action of measuring heights. Readability scores and text statistics were calculated for the original participant information leaflet and for the new assent form using an online tool.⁹⁶ The scores of both PILs are reported in the results chapter.

All participants were provided with information to aid their decision-making that explained both the risks and benefits of orthodontic treatment and participation in the study, as part of the informed consent process. All participants were aged between the ages of 8 and 18 years. For those participants over 16 or deemed 'Gillick competent' consent was obtained from the participant. The participant information leaflet and consent form are attached in Appendices 1 and 2. For those participants under the age of 16 years and not deemed "Gillick competent", consent was obtained from a person of parental responsibility (Appendices 3 and 4) and assent was obtained from the participant (Appendix 5). Informed consent was sought from patients as soon as was reasonably possible after ethical approval for the study had been obtained. A participant information leaflet, describing the study and participants involvement, supplemented the two-stage consent/assent process.

7.4.6 Sample Size

Data were analysed using multiple regression analysis, with CVM stage as a categorical predictor (independent variable), and the velocity of height change as the outcome (dependent) variable. Initially, the sample size was calculated so that if the CVM stage explained at least 7% of the variation in the outcome variable, then a sample size of 164 would allow us to detect a relationship between the predictor and outcome with 80% power at the 95% confidence level.

The sample size was revised based on an interim analysis of collected data, blinded to CVM stage. The standard deviation of the annualised growth velocity was estimated as 5.30cm/yr.

For analysis, patients were grouped into 4 categories, CVM stages 1-2, 3, 4 and 5-6. Franchi et al²⁰ observed growth velocities of approximately 5.5cm/yr, 8.7cm/yr, 5.0cm/yr and 3.4cm/yr in patients starting treatment at these stages. To detect differences between these groups of the magnitude observed in Franchi et al²⁰ with 80% power at the 5% significance level, 17 patients per group would be needed. Therefore the total sample size required was $17 \times 4 = 68$.

7.4.7 Radiograph Exposure

At Liverpool University Dental Hospital, the site for the research study, written procedures that meet the requirements of the Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER)⁸² are in place and local IRMER protocols were followed. All participants underwent radiographic exposure in line with normal clinical practice. Therefore, there was no additional exposure. An expert opinion was sought from Paul Nixon, Consultant in Dental Radiology and Paul Charnock, a medical physics expert who both approved the use of radiographs and declared that the exposure to ionising radiation was reasonable and that the risks were adequately described in the participant and parent information leaflets. In addition, the research ethics committee approved these exposures.

Effective doses and risks for dental examinations are given in Table 7.2 below. This information was taken from the EC publication RP 136 'European guidelines in dental radiology – the safe use of radiographs in dental practice',¹²⁹ but has also been confirmed as appropriate via local output information from the dental units onsite. The data are for adult patients and so assumes a worst-case subject of age 18.

Procedure	No of procedures	Estimated procedure dose (National diagnostic reference levels)	Risk of fatal cancer (per million)
Lateral Cephalogram	1-2	2-3 microsieverts per radiograph (routine for orthodontic treatment)	0.34
OPG	1-2	8 microsieverts per radiograph (routine for orthodontic treatment)	0.21-1.9
Intra oral Radiograph	1	8 microsieverts per radiograph (will only be taken if clinically necessary, not routine)	0.02-0.6

Table 7.2: Ionising Radiation for different radiographs and corresponding risk of fatal cancer

The 'worst-case' patient could have 2 each of panoramic and cephalographic examinations with 1 intra-oral examination. This would result in a typical whole body effective dose of about 30 microsieverts. This equates to an additional risk of fatal cancer of about 1 in 350,000 and is equivalent to the natural background radiation received by members of the public on average during about 1 week.

It is reiterated that all examinations were part of standard care and patients who were not participants in this research study, would also be subject to this level of radiation.

7.4.8 Treatment stopping

All patients were assessed regarding their potential compliance before commencing treatment. However, treatment may have been stopped if the patient failed to comply with attendance at appointments or reached a stage where they compromised the health of their teeth/ gums and the benefits of treatment were outweighed by the consequences.

7.5 Statistics

Statistical support was sought from Dr G. Burnside.

7.5.1 Assessing the validity of CVM staging to predict growth velocity

Data were analysed using multiple regression analysis, with CVM stage as a categorical predictor (independent variable), and height change velocity as the outcome (dependent) variable. The sample size calculation has been described in section 7.4.6.

7.5.2 Cephalometric Method Error

Two methods were used to assess intra-examiner reliability of the lateral cephalograms tracing. The cephalometric tracing error was firstly calculated using Dahlberg's formula:

$$d = \sqrt{\frac{\sum_{i=1}^n (X_{1i} - X_{2i})^2}{2n}}$$

This allowed the calculation of the method error on a random 10% sample of cephalograms. Dahlberg's d is the S.D. of the sample of double determinations, not the average difference. This is a measure of the variability, both random and systematic, due to technical inconsistencies. It is assumed that this value is the same for all specimens and by selecting cases at random to re-measure, it is assumed that the estimate of method error can be extrapolated to the whole sample.

The second method was the British Standards Institution Coefficient of Repeatability (CR) formula advocated by Bland and Altman.¹³⁰ This works on the assumption that the mean difference between two repeated measurements should be zero (if there is large differences between the measurements this method cannot be used). The standard deviation of the differences is measured and if the differences in the measurements lie within two standard deviations for greater than 95% of cases then there is adequate repeatability.¹³¹

7.6 Ethics and Regulatory Approvals

The study was conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements

including but not limited to, the Research Governance Framework and the Medicines for Human Use (Clinical Trial) Regulations 2004, as amended in 2006 and any subsequent amendments.

This protocol and related documents were submitted for review to Liverpool Children's Research Ethics Committee (REC). Amendments were requested to the child information sheet and consent form, which were carried out and submitted. Ethical approval was granted from the Liverpool East Research Ethics Committee, reference number 13/NW/0408 based on protocol number UoL000751; Amendment number 1. This was granted on 30th October 2013.

Annual progress and safety reports and a final report at conclusion of the study were submitted to the sponsor and the REC within the timelines defined in the Regulations.

7.7 Direct Access to Source Data and Documents

The Investigator(s) permitted study-related monitoring, audits, REC review and regulatory inspections (where appropriate) by providing direct access to source data and other documents (i.e. patients' case sheets, X-ray reports etc).

7.7.1 Data Handling

The Chief Investigator (JEH) is acting as custodian for the study data. The following guidelines were strictly adhered to:

All data were collected on a standardised and pseudo-anonymised data collection sheet (Appendix 6). This was kept in the notes of the patient, which were kept in the same records collection area as was usual for all patients undergoing treatment in the orthodontic department.

Any data stored outside the clinical records, was pseudo-anonymised by the allocation of a study identifier. The code for the identifier stored in a locked separate location (SH office). Any radiographic images used were fully anonymised.

All anonymised data were stored on a password-protected computer and all analysis paperwork was kept in a locked drawer in the investigators office, which had a key padlock and was locked at all times.

All study data was stored and archived in line with the Medicines for Human Use (Clinical Trials) Amended Regulations 2006 as defined in the Joint Clinical Trials Office Archiving SOP. After the study has ended, pseudonymised data will be stored on a hospital Trust computer, by the chief investigator, JEH, which will be password protected for 5 years.

7.8 Quality Assurance

Monitoring of this study will be to ensure compliance with Good Clinical Practice and scientific integrity, was managed and oversight retained; by the Co-sponsors (University/Trust).

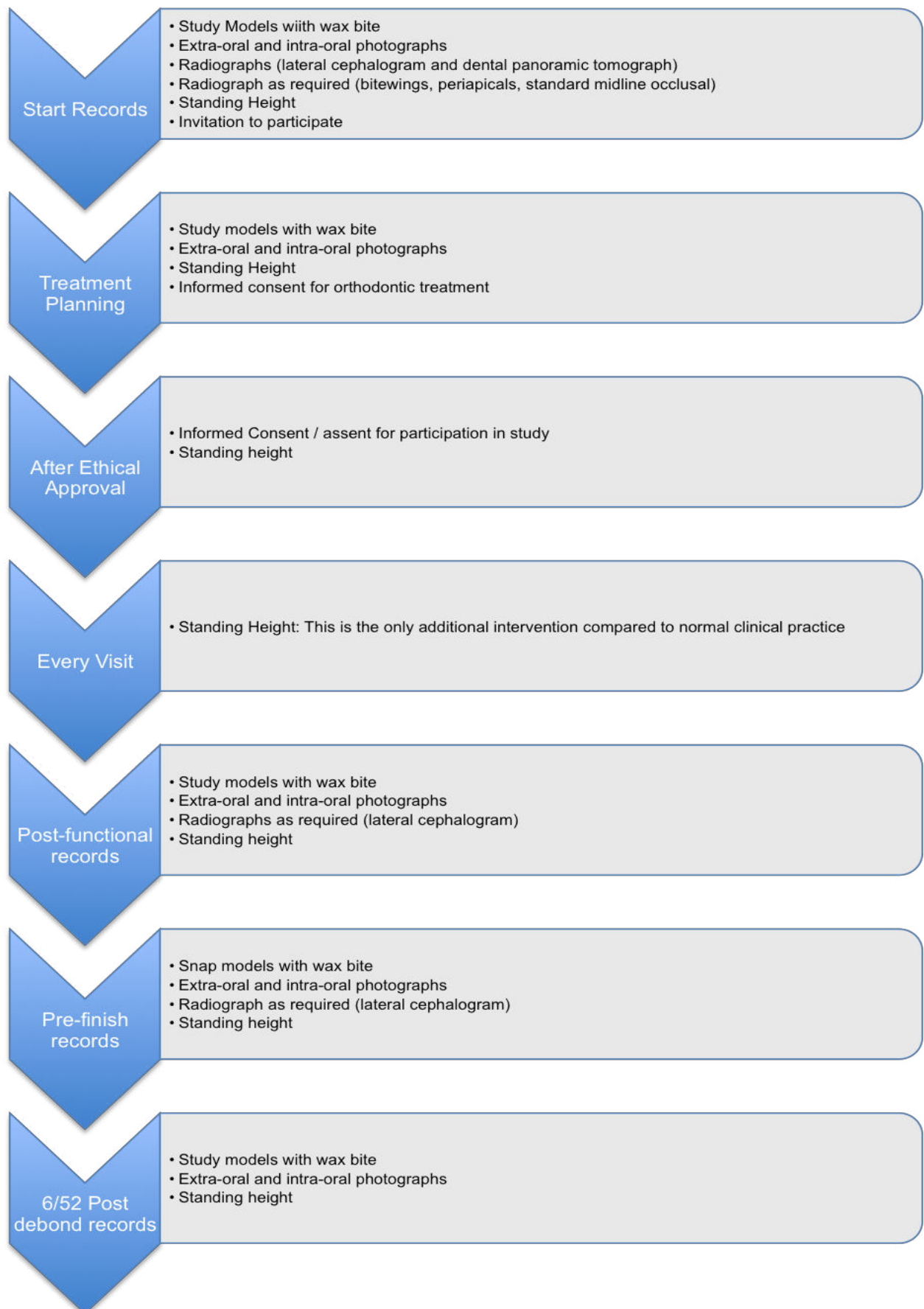
7.9 Publication Policy

It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals. The information also forms part of a research thesis submitted in partial fulfilment of a DDSc at the University of Liverpool.

7.10 Financial Aspects

Small monies were sought from the DDSc research fund (Orthodontic Department) that were used to buy appropriate stationary for the patient information leaflets, and consent/assent forms.

Chapter 8: Summary of Participant Procedures



Chapter 9: Results

9.1 General Characteristics

Patients who met the inclusion criteria and consented to taking part in the study had their first height measured when their initial records were taken or at the soonest appointment after. All initial heights were taken within a maximum of 6 months after the initial lateral cephalogram to ensure that the change in height velocity would reflect the CVM stage assessed on the cephalogram.

Patients heights were then re-measured at every fixed adjust appointment over a 1 year period from the date of ethical approval to the 31st October 2014. Patients that required an additional lateral cephalogram (if it was clinically indicated) were included in the analysis of mandibular growth velocity between the two lateral cephalograms. A second cephalogram was only ordered if the radiograph was indicated clinically and never for the purpose of the research project only.

Inter- and intra-observer reliability was assessed with regards to statural height measurement and CVM staging. The observers involved in statural height measurement were the 1st and 2nd year orthodontic StRs at Liverpool University Dental Hospital. CVM staging was carried out by observer SH. SH was calibrated to observer JH who had been calibrated to CVM images supplied by McNamara, the co-author of the CVM index.

Intra-observer reliability (SH) was also assessed with regards to the three linear measurements that were used to calculate the area of the triangle formed between condylion, gnathion and gonion to calculate mandibular growth.

Regarding the primary outcome, there was a statistically significant increase in statural height velocity at CVM stage 3 when compared to all the other CVM stages. The difference in mean annualised growth velocity was significant between all the CVM stages except between CVM stages 2 and 4.

The amount of mandibular growth that occurred at each CVM stage was higher at stage 3 and 4 than at stages 1, 2, 5 and 6 but due to the small sample size (n=36) this was not statistically significant.

9.2 Readability

After recommendation from the Research Ethics committee to have a patient information leaflet and assent form for the younger age group of 8-12 years, a new PIL was developed with coloured illustrations and improved readability. The readability tests that were applied to assess the ease of reading included, as discussed in the literature review; the Flesch-Kincaid Reading Ease score, the Flesch-Kincaid Grade level, the Gunning-Fog score, the SMOG Index, the Automated Readability Index and the Average Grade Level.

This demonstrated a large change in the readability ease with the average grade level falling from 7.1 to 4.0. A grade level (based on the American school system) is equivalent to the number of years of education a person has had. The Flesch-Kincaid reading ease score increased from 70.6 to 91.6. A higher score indicates easier readability; scores usually range between 0 and 100.

Text Statistics	Old Information Sheet	New Assent Form
Character Count	2,741	1,689
Syllable Count	902	554
Word Count	623	449
Sentence Count	46	42
Characters per word	4.4	3.8
Syllables per word	1.4	1.2
Words per sentence	13.5	10.7

Table 9.1: Text statistics

The calculation of text statistics (Table 9.1) allows the measurement of readability ease using common scoring systems that have described below. This allows the identification of any issues with content readability particularly important in the context of obtaining assent to participate in a research study. It has been shown that a patient's overall satisfaction with their treatment and clinician increases when they understand the information that they have been given.¹³²

Readability Formula	Old Information Sheet	New Assent Form
Flesch-Kincaid Reading Ease	70.6	91.6
Flesch-Kincaid Grade Level	6.8	3.1
Gunning-Fog Score	8.1	5.3
SMOG Index	6.9	3.5
Automated Readability Index	6.1	1.6
Average Grade Level	7.6	4.0

Table 9.2: Readability Scores

In summary, all of the readability scores showed a marked improvement when comparing the original participant information leaflet and the new assent form. The Flesch-Kincaid Grade level with the new assent form was 3.1; this should have been understandable to the youngest patients in our sample. The newly written assent form had a Gunning-Fog index of 5.3, which was a reduction of 2.8 points. The Automated readability index in the new assent form reduced to 1.6 from 6.1. The REC confirmed approval of the changes to the consent form and information leaflet and ethical approval for the study was obtained with the reference number 13/NW/0408 based on protocol number UoL000751 amendment number 1. This was granted on 30th October 2013.

9.3 Reliability

The intra-observer reliability of the CVM index was calculated by construction of a 6x6 table as shown in Table 9.3. These data were entered into the *StatsDirect* App to calculate the linear weighted kappa.

	CVM STAGE AT PHASE I							TOTAL
CVM STAGE AT PHASE II		1	2	3	4	5	6	
	1	7						7
	2		14					14
	3			10				10
	4				19			19
	5					21		21
	6						10	10
TOTAL		7	14	10	19	21	10	81

Table 9.3: 6 x 6 Table for calculating Kappa scores: Example used for SH inter-observer agreement staging LUDH and McNamara's ideal cephalograms

CVM Stage	1	2	3	4	5	6
1	1	0.96	0.84	0.64	0.36	0
2	0.96	1	0.96	0.84	0.64	0.36
3	0.84	0.96	1	0.96	0.84	0.64
4	0.64	0.84	0.96	1	0.96	0.84
5	0.36	0.64	0.84	0.96	1	0.96
6	0	0.36	0.64	0.84	0.96	1

Table 9.4: Cohens Kappa (weighted by $1 - [(i-j)/(1-k)]^2$). Ratings weighted by scale shown.

The weightings shown in Table 9.4 were used to assess the kappa value. The reason for using this weighting is explored in the literature review and exploration of using other weightings is assessed in the discussion chapter.

9.3.1: Intra-observer Reliability of CVM Index

The intra-observer agreement for observer SH for the consecutive image sample from LUDH was 'perfect agreement' with 100% agreement, κ_w 1 SE (0.11). The intra-observer agreement for SH for the ideal sample was also 'perfect agreement' with 100% agreement, κ_w 1 SE (0.33) (Table 9.5).

	Linear weighting				
INTRA-OBSERVER AGREEMENT		% Agreement	K_w	S.E.	95%CI
(OBSERVER SH)	LUDH SAMPLE (72)	100	1	0.11	0.76-1.23
	IDEAL SAMPLE (9)	100	1	0.33	0.34-1.65

Table 9.5: Weighted intra-observer reliability for CVM staging

9.3.2: Inter-observer Reliability of CVM Index

When observers SH and JH were compared, the inter-observer agreement was ‘almost perfect’. The agreement was 97.4% with the LUDH sample (K_w 0.83) and 99.3% agreement with the ideal image sample. (K_w 0.96) (Table 9.6).

	Linear weighting				
INTER-OBSERVER AGREEMENT		% Agreement	K_w	S.E.	95%CI
OBSERVERS SH & JH	LUDH SAMPLE (72)	97.4	0.83	0.11	0.61-1.07
	IDEAL SAMPLE (9)	99.3	0.96	0.32	0.32-1.61

Table 9.6: Inter-observer reliability of CVM index (SH and JH)

9.3.3: Validation of the McNamara CVM teaching method

The ideal image sample was provided by the co-author of the index, Professor J McNamara and each image represented a distinct CVM stage. Assessing the agreement between the observers when they applied the index to the ideal image sample was used to validate the CVM teaching method described by McNamara. The agreement with this sample was overall ‘almost perfect’. The intra-observer agreement was 100%, K_w 1 SE (0.33) (SH). The inter-observer agreement was 99.3%, K_w 0.96 SE (0.32) (SH and JH). The high level of agreement with the ideal image sample suggests that observers were able to apply the CVM staging method in the way it was intended.

9.3.4: Calibration of LUDH researchers SH and JH as CVM experts

In order for SH to be calibrated in this method of CVM staging, SH was calibrated against a sample of lateral cephalograms that had been used in previous research looking at the reliability of the CVM method.²⁷ In Rainey's reliability study, mutually agreed CVM stages for each radiograph in a sample from LUDH was compared to the CVM stage determined by the authors of the index, Dr. J McNamara and Dr. L Franchi. The overall agreement between the 2 results was 'substantial' 93% K_w 0.78 SE (0.03). The upper limit of the 95% confidence interval fell in the 'perfect agreement' category. This confirmed the LUDH researchers had an acceptable level of agreement with the authors of the index to be awarded 'expert' status.

The same sample was used to calibrate SH and her reliability using this method. The overall agreement with JH was 97.4% K_w 0.83, falling within the 'perfect agreement category' thus establishing researcher SH as calibrated in using the method.

9.3.5: Reliability of Height Measurement

To determine the reliability of the 8 registrars taking the standing height measurements, all 8 observers measured 20 members of staff from the orthodontic department on two occasions 6 weeks apart. The height measurements took place at the same time of day (morning) on the same week day on both occasions as it has been documented that people's statural height changes depending on the time of day and day of the week.¹³³

The order that people were measured was randomised using a computer-generated list (generated by JEH) in an attempt to reduce bias. The observers were blinded to each other's measurements to reduce any bias. Both intra-class correlation coefficients and Bland and Altman plots were used to assess intra- and inter-observer agreement.

9.3.6: Intra-observer Reliability of Statural Height Measurement

SH

The intra-class correlation coefficient (one way random effects) was 0.994 (SD=0.54), which as classed as excellent agreement. This is demonstrated in Figure 9.1.

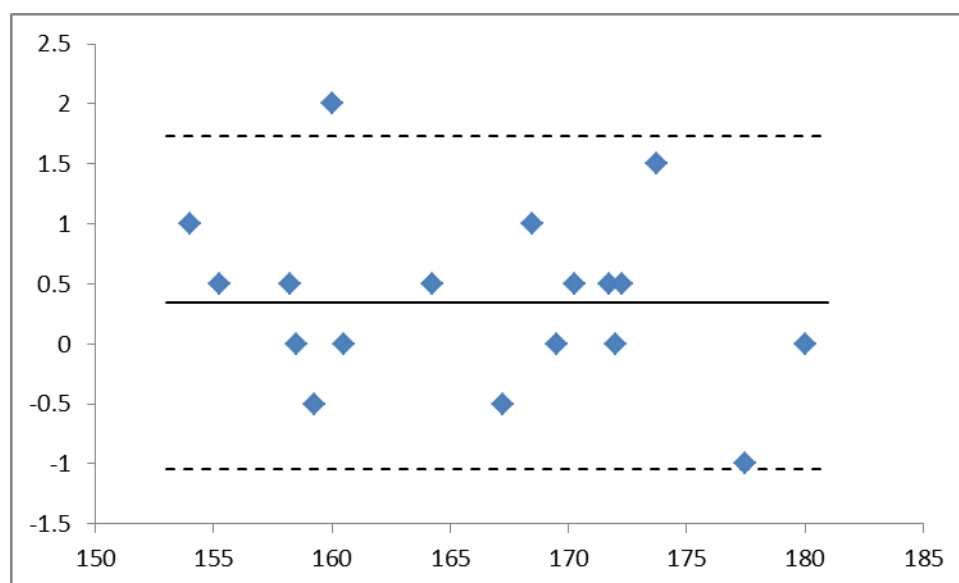


Figure 9.1: Bland and Altman Plot for SH intra-observer agreement for standing height measurement; Mean difference: 0.34, Limits of agreement: -1.05 - 1.73.

Statistics	Intra-class correlation coefficient (ICC)	Mean Difference	Limit of agreement
StR			
SH	0.994	0.34	-1.05, 1.73
StR 1	0.996	0.32	-0.85, 1.49
StR 2	0.993	0.51	-0.77, 1.79
StR 3	0.993	0.53	-0.72, 1.77
StR 4	0.994	0.18	-1.13, 1.50
StR 5	0.997	0.22	-0.79, 1.23
StR 6	0.995	0.13	-1.43, 1.69
StR 7	0.994	0.45	-0.83, 1.73

Table 9.7: Table to summarise all StRs results for reliability of statural height measurements including intra-class correlation coefficient (one way random effects) for inter-observer agreement as well as the mean difference and limits of agreements from the Bland and Altman Plots for intra-observer agreement for standing height measurement.

9.3.7: Inter-observer Reliability of Statural Height Measurement

Phase 1: First stage calibration of StRs for measurement of statural height

The intra-class correlation coefficient (one way random effects) for inter-observer agreement of standing height measurements was 0.986, which is classed as excellent. This is displayed in an agreement plot in Figure 9.2.

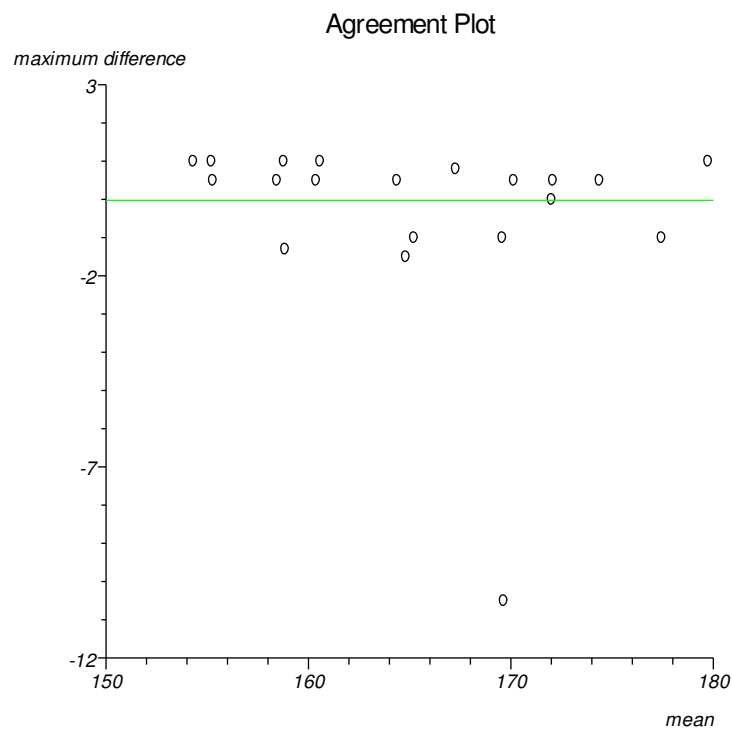


Figure 9.2: Bland and Altman Plot for inter-observer agreement for standing height measurement at Phase 1

Phase 2: Second stage of calibration of StRs for statural height measurements

The intra-class correlation coefficient (one way random effects) for inter-observer agreement of standing height measurements was 0.997, which is classed as excellent. This is displayed in an agreement plot in Figure 9.3.

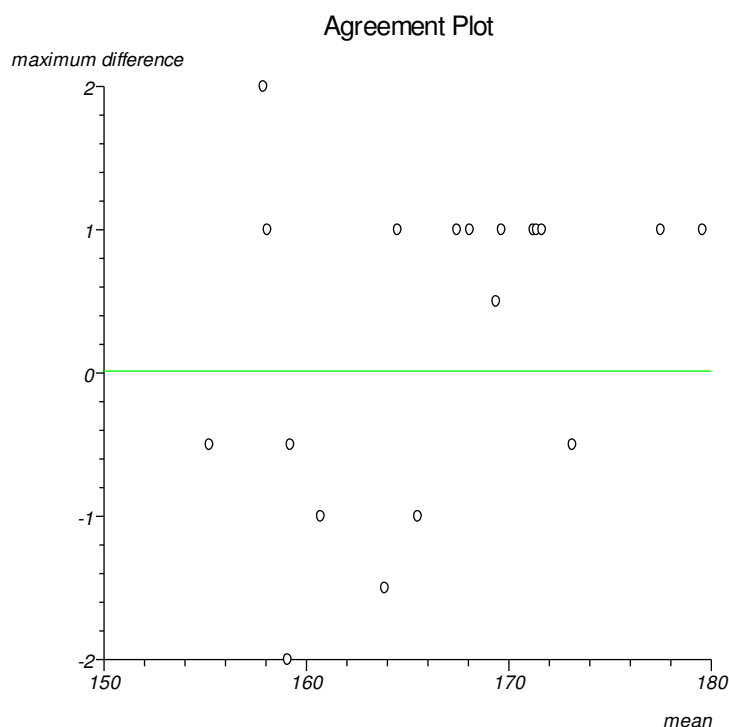


Figure 9.3: Bland and Altman Plot for inter-observer agreement for standing height measurement at phase 2

9.3.8: Intra-observer Reliability of Cephalometric Measurements

To assess the reliability of cephalometric measurements, observer SH measured 20 cephalograms 6 weeks apart. The 20 lateral cephalograms used to assess the reliability were selected at random by JEH from an original sample of 130 lateral cephalograms using a computer generated randomised sequence in an attempt to reduce selection bias.

Lines condylion-gonion, gonion-gnathian and gnathian-condylion were measured on these 20 radiographs, as they were used to calculate the area of the triangle made by these three landmarks to assess mandibular size. The rationale for using these landmarks to assess mandibular growth was explored in the literature review.

9.3.8.1 Intra-observer Reliability of Condylion-Gonion

Condylion – Gonion Agreement

The Intra-class correlation coefficient (one way random effects) was 0.93 (SD 0.17), which is classed as excellent. Agreement was also plotted on a Bland and Altman plot (Figure 9.4)

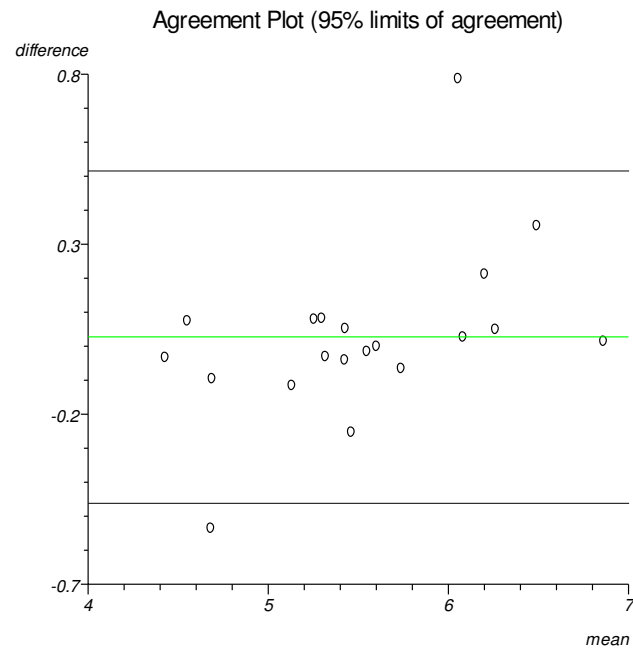


Figure 9.4: Bland and Altman Plot for SH intra-observer agreement for condylion-gonion linear measurement, 95% Limits of agreement = -0.46 to 0.52

9.3.8.2 Intra-observer Reliability of Gonion-Gnathion

The intra-class correlation coefficient (one way random effects) was 0.93 (SD 0.12), which is classed as excellent. Agreement was also plotted on a Bland and Altman plot (Figure 9.5)

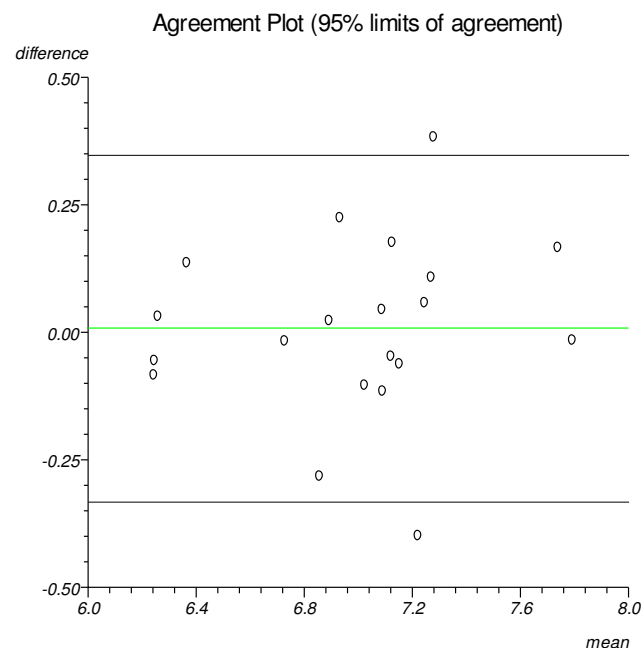


Figure 9.5: Bland and Altman Plot for SH intra-observer agreement for gonion-gnathion linear measurement, 95% Limits of agreement = -0.33 to 0.35

9.3.8.3 Intra-observer Reliability of Gnathion - Condylion

The intra-class correlation coefficient (one way random effects) was 0.85 (SD 0.31) which although lower than the other 2 linear measurements is still classed as excellent. Agreement was also plotted on a Bland and Altman plot (Figure 9.6).

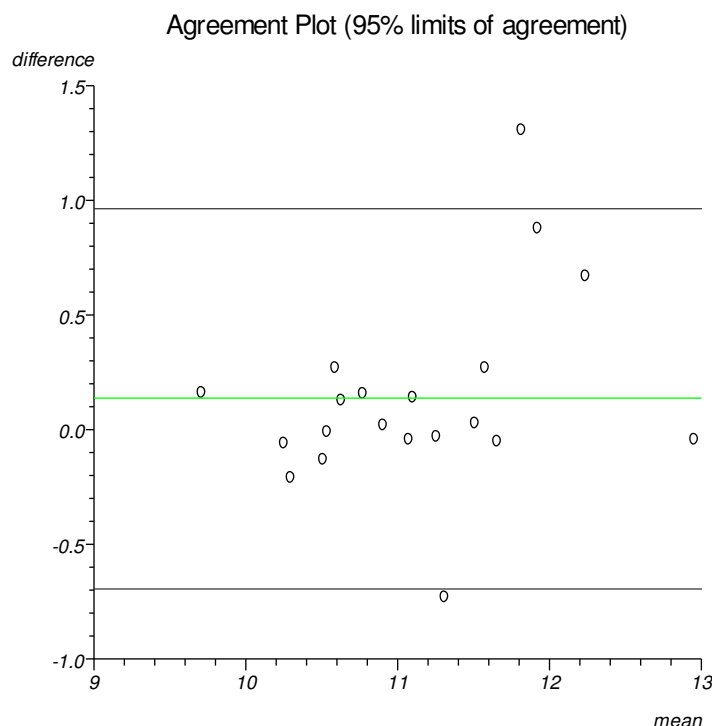


Figure 9.6: Bland and Altman Plot for SH intra-observer agreement for gnathion-condylion linear measurement, 95% Limits of agreement = -0.69 to 0.97

9.4: Descriptive Statistics of Sample

The total number of patients recruited into the study was 185. In the process of data collection, 6 patients had to be excluded due to the second, third and fourth vertebrae not all being visible on the radiograph. This is a potential problem with using the CVM index that had been identified previously and will be examined further in the discussion section.

Only one height measurement had been recorded for 26 patients, and thus, these patients had to be excluded from the study, as no annualized growth velocity could be calculated. This problem stemmed from data collection and despite frequent reminders to those taking part in the study, not all were diligent in taking the height measurements for their patients.

The inclusion criteria included patients of age 8-18 years, so 4 patients had to be excluded from the study, as they were aged 19-30 years old. It is interesting to note that no patients

were excluded for being too young, but this is probably a reflection of the population that were most commonly treated.

On collating the data, it emerged that some patients had not had their standing height measured at the time of their first cephalometric radiograph. This was not seen to be a problem if the first height was measured a few months after the radiograph. However, there were a number of patients where the first height was recorded 2 years after the initial lateral cephalogram. On discussion it was felt that these had to be excluded from the data analysis as the height change 2 years after the cephalogram may not reflect the CVM stage recorded on the cephalogram. With this in mind, any patients who had not had their heights measured within 6 months of having their initial lateral cephalogram taken were excluded from the final analysis, which caused a further 41 patients to be excluded. Thus, the final sample size that could be used in the data analysis was 108. This is demonstrated in Figure 9.7, which shows the flow of patients through the study.

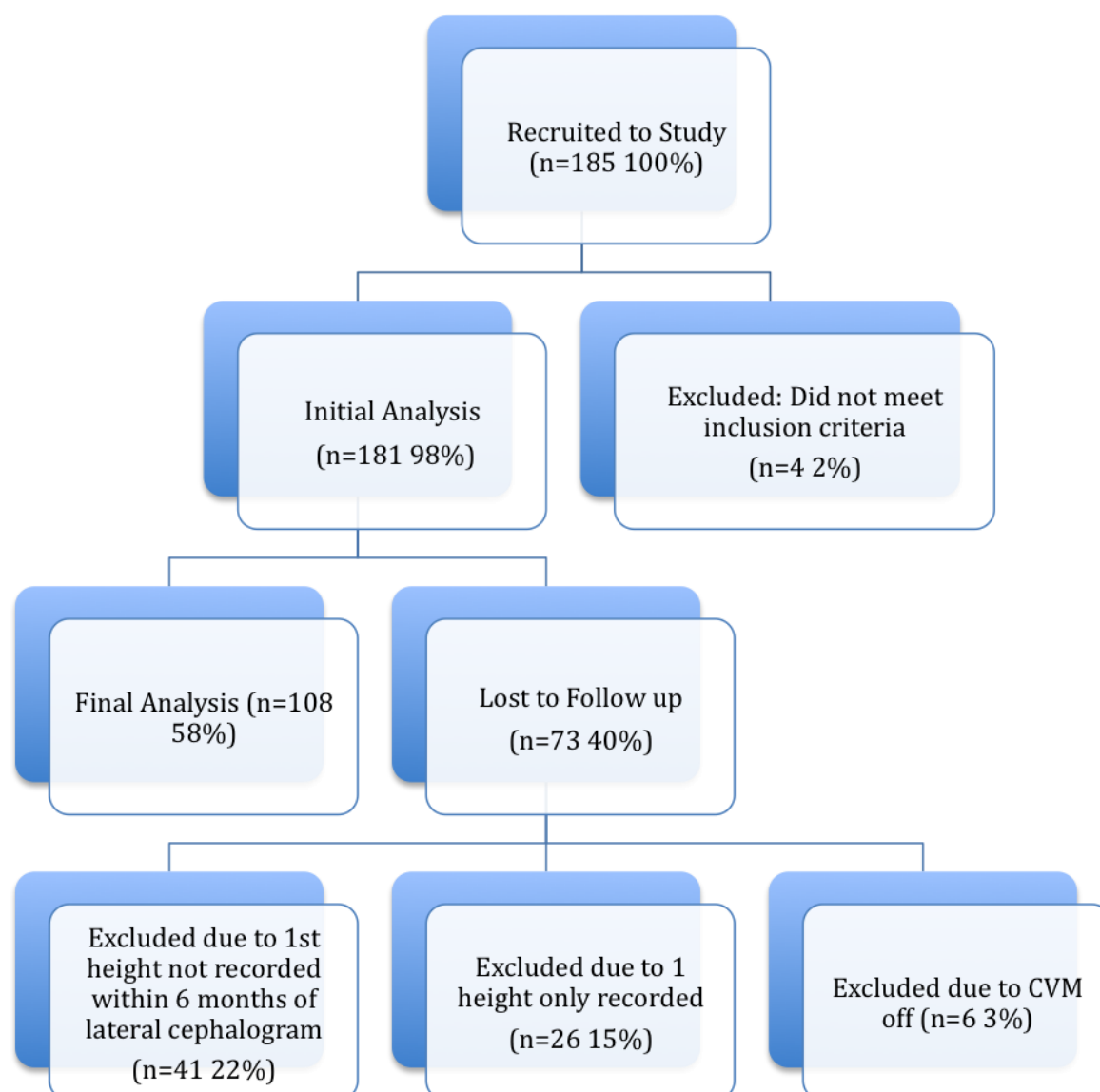


Figure 9.7: Flow diagram of participants in study

The mean age in the final sample (n=108) was 13.9 years (SD=1.7) (Table 9.8) and ranged from 10.16 years to 18.56 years. The age distribution was normal as shown in Figure 9.8.

	Number of Patients	Mean	Minimum	Maximum	95% CI		Standard Deviation
					Lower Bound	Upper Bound	
Age (years)	108	13.97	10.16	18.56	13.64	14.30	1.7

Table 9.8: Mean age and age range of study participants.

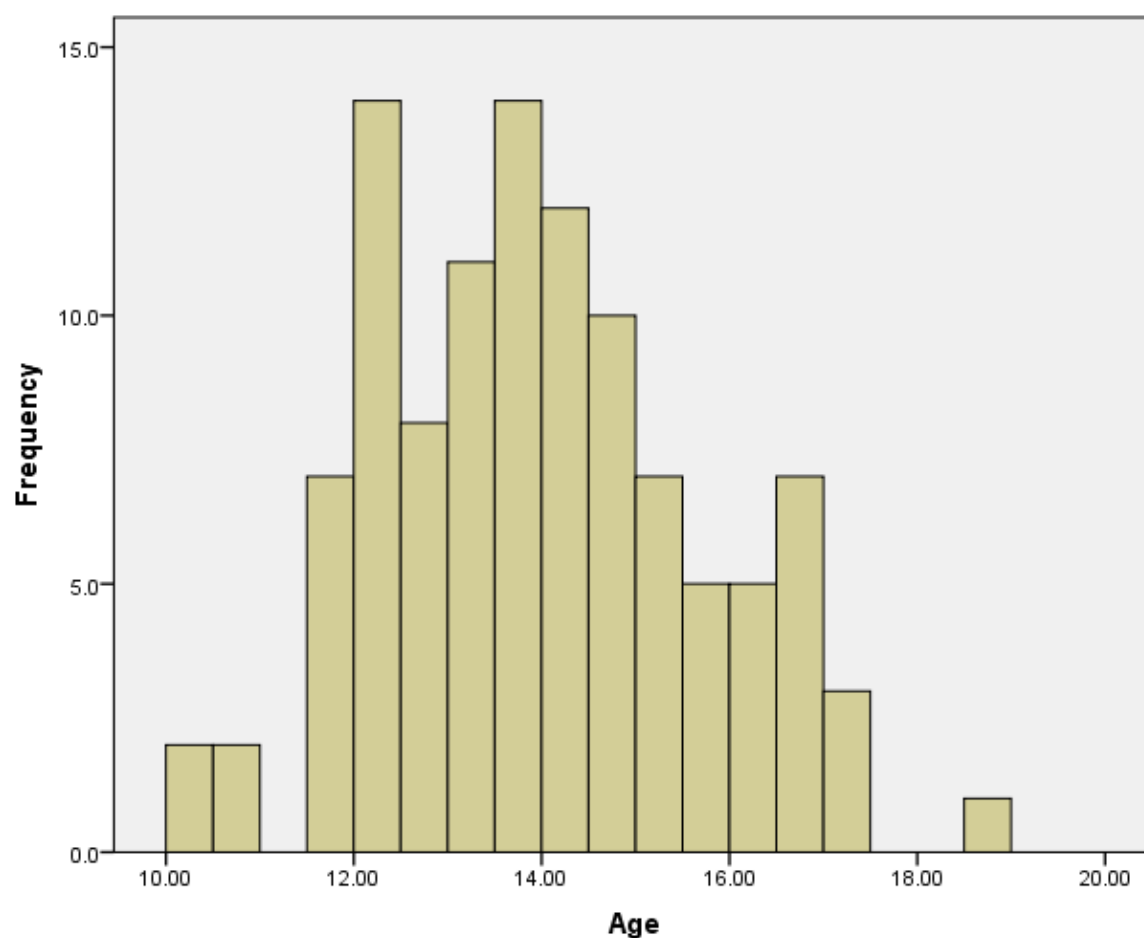


Figure 9.8: Age distribution of patients included in final analysis

There were 60 females (56%) and 48 males (44%) in the final sample (Table 9.9). The mean age within the females was 13.5 years (age range 10.16-17.35 years SD 1.6). The mean age in the males was 14.5 years (age range 11.8-18.56 years SD 1.6). As the difference between the males and females was not significant, they were analysed together.

Gender	Number of Patients	Mean	Standard Deviation	Minimum	Maximum	95%CI	
						Lower Bound	Upper Bound
Female	60	13.51	1.62	10.16	17.35	13.10	13.93
Male	48	14.53	1.64	11.80	18.56	14.06	14.22
Total	108	13.97	1.70	10.16	18.56	13.64	14.30

Table 9.9: Table to show breakdown of males and females and their age distribution

In order to have enough patients in each group to demonstrate enough power to show a statistically significant difference, patients at CVM stages 1 and 2 were combined and CVM stage 5 and 6 were combined. In addition, it is the middle stages that are of particular interest for the purpose of this research.

When the patients who had not had their height recorded within 6 months of their lateral cephalogram being taken were excluded, this excluded a further 41 patients from the participants that were eligible to be included in the analysis.

Table 9.10 shows the number of patients at each CVM stage. The group with the highest number of patients was CVM stage 5 followed by 4. The groups with the lowest frequencies were CVM stage 1 followed by CVM stage 6.

CVM stage	Number of patients	Percentage	Cumulative Percentage
1	1	0.9	0.9
2	13	12.0	13.0
3	22	20.4	33.3
4	33	30.6	63.9
5	34	31.5	95.4
6	5	4.6	100.0
Total	108	100.0	

Table 9.10: Number and Percentage of patients in final sample at each CVM stage

When the patients at CVM stages 1 and 2 and stages 5 and 6 were combined the new frequencies at each stage are shown in Table 9.11. The sample size required to give adequate power was reached in all the groups except group CVM stage 1 and 2 which had 3 participants fewer than the target sample size of 17.

CVM Stage	Number of Patients	Percentage	Cumulative Percentage
1 & 2	14	13.0	13.0
3	22	20.3	33.3
4	33	30.6	63.9
5 & 6	39	36.1	100.0
Total	108	100.0	

Table 9.11: Number and Percentage of patients in final sample at each stage, when CVM stages 1&2 and 5&6 combined

It is interesting to note the distribution of males and females at each CVM stage (Table 9.12). It has been documented previously that females reach puberty prior to males and this is reflected in this sample. A much higher proportion of the females were at CVM stage 4 and 5, whereas a larger proportion of the males are at CVM stage 3 and 4 within this particular snapshot in time.

Gender		CVM Stage						
		1	2	3	4	5	6	Total
Female	No.	0	9	8	17	24	2	60
	%	0	15	13	28	40	3	
Male	No.	1	4	14	16	10	3	48
	%	2	8	29	33	21	6	
Total	No.	1	13	22	33	34	5	108
	%	1	12	20	31	31	5	

Table 9.12: Number and Percentage of patients at each CVM stage broken down in to male and female

9.5: CVM Stage and Statural Height Velocity

For ease the group combining CVM stages 1 and 2 will be referred to as Stage 2. The group combining CVM stages 5 and 6 will be referred to as Stage 5. (Stage 3 represents CVM stage 3 and stage 4 represents CVM stage 4).

Table 9.13 shows the mean annualised growth velocity (MAGV) in centimetres per year (cm y^{-1}) in each CVM group. There was an increase in the MAGV from stage 2 to stage 3 by almost 5cm. The MAGV then drops by 4.3cm at CVM stage 4 relative to CVM stage 3. At stage 5, the MAGV drops further by 3.5cm to 1.5cm MAGV. This pattern would support the idea that standing height velocity is greatest at CVM stage 3.

CVM Stage	Mean annualized growth rate (cm y^{-1})	Number of patients	Standard deviation
1 & 2	4.51	14	2.71
3	9.39	22	4.44
4	5.00	33	2.33
5 & 6	1.56	39	2.34
Overall/Total	4.59	108	4.06

Table 9.13: Mean annualised growth velocity by CVM stage

The trend in MAGV through the CVM stages is displayed in Figure 9.9. This demonstrates the increase in MAGV that occurs at CVM stage 3. The growth velocity then decreases at CVM stage 4 from CVM stage 3, and further reduces going into CVM stage 5 and 6. There were 2 outliers in the CVM stage 3 group who showed a particularly high rate of growth. There are also 3 outliers at CVM group 5 and 6, which suggests that there were individuals who displayed some late growth.

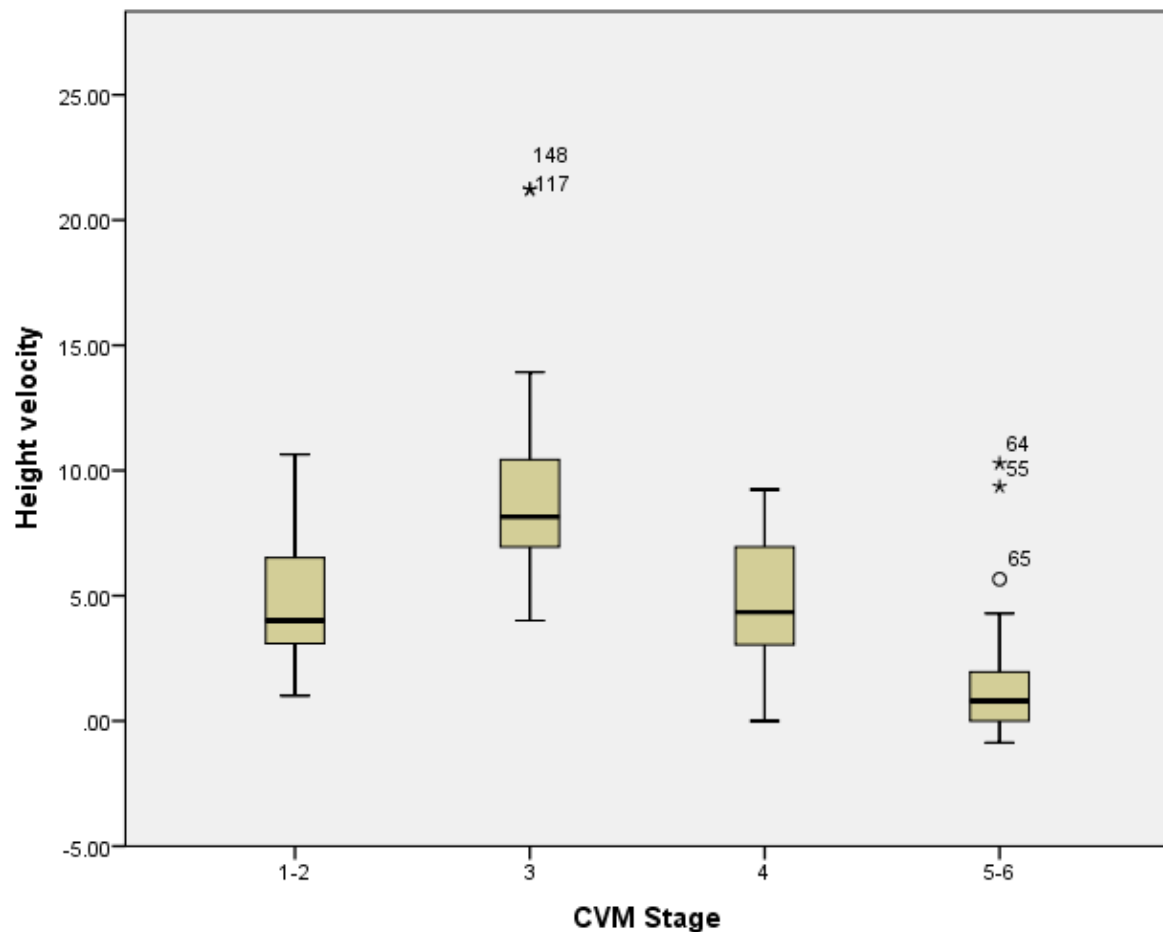


Figure 9.9: Box plot of mean annualised growth velocity MAGV at different CVM stages

When assessing the MAGV split between gender (Tables 9.14, 9.15), the same pattern is seen as described above with the MAGV highest at CVM stage 3 and decelerating towards CVM stage 5. However, males' growth velocities were generally higher than females and their peak growth velocity was $10.4\text{cm}\cdot\text{y}^{-1}$ (95%CI: 7.68, 13.30) MAGV compared to only $7.5\text{cm}\cdot\text{y}^{-1}$ (95%CI: 4.83, 10.26) MAGV for girls; but this difference was not statistically significant in our sample ($p=0.36$).

CVM Stage	Mean annualized growth rate (cmy ⁻¹)	Number of patients	Standard deviation	95% Confidence Interval	
				Lower Bound	Upper Bound
1 & 2	3.87	9	2.16	2.21	5.53
3	7.54	8	3.25	4.83	10.26
4	4.43	17	2.20	3.31	5.57
5 & 6	1.77	26	2.70	0.68	2.86
Overall /Total	3.61	60	3.17		

Table 9.14: Mean annualised growth velocity at each CVM group for Females

CVM Stage	Mean annualized growth rate (cmy ⁻¹)	Number of patients	Standard deviation	95% Confidence Interval	
				Lower Bound	Upper Bound
1 & 2	5.65	5	3.47	1.34	9.96
3	10.44	14	4.79	7.68	13.20
4	5.60	16	2.38	4.33	6.87
5 & 6	1.13	13	1.39	0.29	1.97
Total	5.81	48	4.70		

Table 9.15: Mean annualised growth velocity at each CVM group for Males

Table 9.16 shows the mean age at each CVM stage. The difference between the ages at each CVM stage was not significant except for between stages 5/6 and all the other CVM stages.

When females and males were looked at separately, the same pattern was found, that the difference in age between stages 1-2, 3 and 4 were not significant; however, the difference between stages 5 and 6 and the other stages was significant.

CVM Stage	Mean age (yrs)	Standard deviation	95% Confidence Interval	
			Lower Bound	Upper Bound
1 & 2	12.71	1.22	12.01	13.41
3	13.15	1.12	12.65	13.65
4	13.55	1.57	13.00	14.11
5 & 6	15.23	1.45	14.76	15.70

Table 9.16: Average age in years at each CVM stage

The mean age of females at CVM stage 3 was 12.4 (SD 1.4) years whereas males were an average age of 13.5 (SD 0.9) years when they were at CVM stage 3 as shown in Table 9.17. This confirms previous research reporting that females reach puberty prior to males and the difference was significant [-1.20cm (95%CI -2.12, -0.28)].²⁰

Gender	Number of Patients	Mean Age (years)	Minimum	Maximum	95%CI		Standard Deviation
					Lower Bound	Upper Bound	
Female	8	12.4	10.55	13.61	11.46	13.36	1.14
Male	14	13.6	11.80	14.51	13.06	14.09	0.90
Total	22	13.2	10.55	14.51	12.65	13.65	1.12

Table 9.17: Average age of males and females at CVM stage 3

ANOVA was used to test for statistically significant differences in the MAGV between the different CVM stages. The null hypothesis stating that there was no difference between the 4 groups was rejected, with the differences being statistically significant to a p-value of 0.0001 (Table 9.18).

	Sum of squares	df	Mean Square	F	Sig
Between Groups	869.662	3	289.887	33.812	0.0001
Within Groups	891.657	104	8.574		
Total	1761.319	107			

Table 9.18: ANOVA results testing null hypothesis of no difference between the 4 CVM stage groups with regards to MAGV was rejected. The P-value of 0.0001 suggests there was a significant difference between the MAGV of patients at different CVM stages.

Pairwise comparisons were then carried out (Table 9.19) to look at each stage relative to every other stage and look for statistically significant differences.

Firstly starting with CVM Stage 2, there was a statistically significant difference from Stage 3 with Stage 2 being on average 4.88cm yr^{-1} less ($p=0.001$, 95%CI 2.26;7.49). There is also a statistically significant reduction (of 2.9cm yr^{-1}) in MAGV between Stage 2 and Stage 5 ($p=0.001$, 95%CI 0.56;5.32). However, the difference in MAGV between Stage 2 and Stage 4 was not statistically significant.

Looking at CVM Stage 3, the MAGV at CVM Stage 3 was significantly higher than the MAGV at all the other stages. The difference between Stage 3 and Stages 2 and 4 were very similar (4.88cm yr^{-1} and 4.38cm yr^{-1}) whereas the difference between Stage 3 and Stage 5 was slightly larger with the MAGV at Stage 3 being on average 7.8cm yr^{-1} higher than the MAGV at Stage 5.

Looking at CVM Stage 4 compared to the other stages, there was no significant difference between the MAGV at Stage 2 and Stage 4. The MAGV at Stage 3 was an average of 4.4cm yr^{-1} higher than at Stage 4 ($p=0.0001$, 95%CI 2.28;6.49). The MAGV at Stage 5 was an average of 3.4cm yr^{-1} lower than at Stage 4 ($p=0.001$, 95%CI 1.63;5.25).

Looking at Stage 5, the MAGV was significantly lower at this stage than any other group, but particularly lower than the MAGV at Stage 3 (a difference of 7.8cm yr^{-1} ($p=0.001$, 95%CI 5.79;9.86)).

CVM Stage (A)	CVM Stage (B)	Mean Difference (A-B)	Std. Error	Significance	95% Confidence Interval	
					Lower Bound	Upper Bound
2	3	-4.88	1.00	0.001*	-7.50	-2.27
	4	-4.97	0.93	0.951	-2.93	1.94
	5	2.94	0.91	0.009*	0.56	5.33
3	2	4.88	1.00	0.001*	2.27	7.50
	4	4.38	0.81	0.001*	2.28	6.49
	5	7.83	0.78	0.001*	5.79	9.86
4	2	0.50	0.93	0.951	-1.94	2.94
	3	-4.38	0.81	0.001*	-6.49	-2.28
	4	3.44	0.69	0.001*	1.63	5.25
5	2	-2.94	0.91	0.009*	-5.33	-0.56
	3	-7.83	0.78	0.001*	-9.86	-5.79
	4	-3.44	0.69	0.001*	-5.25	-1.63

*The mean difference is significant at the 0.05 level.

Table 9.19: Pairwise comparisons of differences between stages. Dependant variable: Mean annualized growth velocity. Tukey HSD

9.6: CVM Stage and Mandibular Growth Velocity

The participants who had had two lateral cephalograms taken by the end date of the study were included in the analysis to determine velocity of mandibular growth. Table 9.20 shows the number of patients at each CVM stage at the time of their initial lateral cephalogram. There were a total of 36 participants who had 2 cephalograms taken.

CVM Stage	Number of Patients	Percentage	Cumulative Percentage
1	1	2.8	2.8
2	4	11.1	13.9
3	11	30.6	44.4
4	8	22.2	66.7
5	12	33.3	100
Total	36	100	

Table 9.20: Number and Percentage of patients at each CVM stage

Table 9.21 shows the frequencies in each category when Stages 1 and 2 and combined and Stages 5 and 6 were combined as done previously. Despite combining the first two and last two stages, the numbers in each group were not sufficient to detect any statistically significant differences despite some clear trends emerging.

CVM Stage	Number of patients	Percentage	Cumulative Percentage
1 & 2	5	13.9	13.9
3	11	30.6	44.4
4	8	22.2	66.7
5 & 6	12	33.3	100
Total	36	100	

Table 9.21: Number and Percentage of patients at each CVM group when CVM stages 1 and 2 and CVM stages 5 and 6 were combined

Table 9.22 shows the change in the area of the triangle formed by Go-Co-Gn annualised so that the velocity of growth is standardised and can be compared between stages. The mandibular growth velocity was the lowest in stage 2 (0.19cm^2) followed by stage 5

(0.26cm²) followed by stage 4 (0.446cm²) with the highest growth velocity at stage 3 (0.448cm²).

All the linear measurements (Co-Go, Go-Gn, Gn-Co) showed a similar pattern with stage 3 showing the highest velocity of growth, closely followed by stage 4. The velocity of growth is higher at stage 5 than stage 2 for line gonion-condylion. However, it was the converse with both condylion-gnathion and gonion-gnathion where the growth velocity was lowest at stage 5 followed by stage 2.

CVM Stage		Area of Triangle Co-Go-Gn (cm ² y ⁻¹)	Condylion-Gnathion (cm ² y ⁻¹)	Gnathion-Gonion (cm ² y ⁻¹)	Gonion-Condylion (cm ² y ⁻¹)
1 & 2 (N= 5)	Mean	0.19	0.38	0.13	0.19
	Std. Deviation	0.24	0.32	0.12	0.25
3 (N= 11)	Mean	0.45	0.54	0.17	0.45
	Std. Deviation	0.29	0.29	0.31	0.39
4 (N= 8)	Mean	0.45	0.54	0.16	0.45
	Std. Deviation	0.37	0.28	0.32	0.37
5 & 6 (N= 12)	Mean	0.26	0.26	0.08	0.26
	Std. Deviation	0.45	0.48	0.21	0.45
Overall (N= 36)	Mean	0.35	0.42	0.13	0.35
	Std. Deviation	0.39	0.38	0.25	0.39

Table 9.22: Mean change in annualised area of triangle Co-Go-Gn, and linear measurements Co-Gn, Gn-Go, and Go-Co.

An ANOVA statistical test was carried out to test for differences between the groups but none of the stages were shown to have a statistically significant difference in velocity of mandibular growth, due to the small numbers involved (Table 9.23).

Change per year		Sum of Squares	df	Mean Square	F	Sig.
Area of triangle Co-Go-Gn	Between groups	0.41	3	0.14	0.87	0.47
	Within Groups	4.95	32	0.16		
	Overall	5.35	35			
Condylion-Gnathion	Between groups	0.58	3	0.19	1.43	0.25
	Within Groups	4.33	32	0.14		
	Overall	4.91	35			
Gnathion-Gonion	Between groups	0.06	3	0.02	0.29	0.84
	Within Groups	2.20	32	0.07		
	Overall	2.26	35			
Gonion-Condylion	Between groups	0.41	3	0.14	0.87	0.47
	Within Groups	4.95	32	0.16		
	Overall	5.35	35			

Table 9.23: ANOVA testing null hypotheses of no difference between groups with regards to annualised mandibular growth velocity.

Chapter 10: Discussion

Growth is such a fundamental concept in orthodontics, that it is not uncommon for the decision regarding timing or even modality of treatment to be influenced by the stage of growth and development of the patients.

Peak growth velocity in standing height has been shown to be one of the most accurate methods of determining the overall skeletal growth velocity.^{13, 33} However, this is not useful to the orthodontist who can only assess the peak growth velocity in standing height retrospectively and it is of little assistance when it comes to assessing the remaining growth potential. In addition, this would require regular measurements of a patient's standing height which is not practical because the orthodontist often doesn't see the patient regularly at the appropriate stage, only seeing them as a new patient when referred by their dentist with a desire for orthodontic treatment.

Assessment of the morphology of the cervical vertebrae, using various indices has been proposed as a method of identifying the timing of onset of the pubertal peak in skeletal growth, and estimates the proportion of growth remaining.^{16, 20, 26} However, no previous research has prospectively demonstrated a significant correlation between the CVM stage and standing height growth velocity in a contemporary sample of children and adolescents. The results of this research study have confirmed the findings of previous retrospective research based on historic samples. This has been contrary to the expectations of the primary researcher. This may have potentially significant clinical implications, which will be explored throughout the discussion chapter.

10.1 Limitations of the study

10.1.1 Ethical Approval

Ethical approval took approximately one year to obtain which delayed the start of data collection and reduced the duration for which the study could run. Due to the restricted time period over which the research can be carried out due to it being tied to a 3 year DDSc programme, the delay in obtaining ethical approval meant that the data collection could only run for 1 year. There were many barriers to the smooth progress of the process of obtaining ethical approval for the study.

Despite the only intervention being the measurement of patients' heights, a full ethical review was required including an interview with the Research Ethics Committee (REC). An expert opinion and risk report was required from both a consultant radiologist and a nuclear

physicist because radiographs were being assessed as part of the research. This was despite the fact that no radiographs were being taken for the purpose of the research. We were using radiographs that had already been taken as part of the patients' treatment planning process and were only taken when clinically indicated and justifiable, but never for the purpose of this study alone. These issues, in addition to administrative delays and IT issues with the IRAS website, contributed to the lengthy process of obtaining ethical approval.

This was further compounded by the Research Ethics Committee's request to change the consent forms and the subsequent amendment submitted to extend recruitment and allow the following cohort of StRs to recruit patients for the study.

10.1.2 CVM not present on lateral cephalogram

In total there were 6 patients who had to be excluded from the final analysis, despite having several heights recorded, due to the vertebrae (C2, C3 and C4) not being present on the radiograph. This meant that it was not possible to use the radiographs and apply the CVM index. This highlights the importance of liaising with radiology departments to ensure that staff are aware of the correct patient positioning required when taking a lateral cephalogram to ensure that the second, third and fourth vertebrae are included on the lateral cephalogram. This issue was highlighted in the audit that was carried out and reported in Chapter 4.

10.1.3 Patients not meeting inclusion criteria

Patients who were not included in the data analysis due to not meeting the inclusion criteria totalled 4; all of these were due to the patient being too old, the ages of these 4 patients ranged from 19 to 30 years old. Despite the StRs involved being briefed on the inclusion criteria, it was inevitable that a few patients were recruited by mistake as a result of over enthusiastic recruitment. With the benefit of hindsight, it may have been worth including a checklist of the inclusion and exclusion criteria, in each surgery to serve as a reminder to the recruiting registrars; this may have reduced the number of patients recruited in error.

10.1.4 First height not recorded within 6 months of lateral cephalogram

The largest cause of patients having to be excluded from the analysis was due to lack of recorded information. The StRs involved were asked to record the height of the patient at the time their initial records were taken, and then after ethical approval had been obtained, at every appointment the patient attended. There were two main issues that were major limitations in the study. The first was that StRs did not always record the height of the patient

when they had their first cephalogram taken. This was not a problem if they recorded the height a few weeks later or even a few months later. However, there was a large number (n=41) where the height was not recorded for more than 6 months after the initial cephalogram. This meant that it was not possible to say for certain that the patient was at the CVM stage recorded on the radiograph when the first height was recorded. To ensure that this did not bias the results, any patients who had not had their first height recorded within 6 months of having their cephalogram taken were excluded. This unfortunately resulted in 41 patients being excluded from the final analysis and meant that the ideal sample size of 17 in the group, was not obtained for patients who were at CVM stages 1 and 2.

10.1.5 Patients with only one height recorded

Another large limitation of this study related to data collection, was that many patients only had one height recorded. This meant that it was not possible to calculate an annualised growth velocity for these patients and thus they had to be excluded (n=26).

Thus, in total, 77 patients had to be excluded from the final analysis, due to height measurements not being taken at the appropriate time(s). This was a substantial loss and their inclusion would have significantly increased the power of the study. It is however, a frequently encountered limitation of this type of research. Data collection depends on people without a vested interest in the study, collecting the data, and despite frequent reminders, the reality of busy clinics and being in a learning environment meant that it was inevitable that sometimes height recording was forgotten. If doing a similar study in the future, it may be of value to include a checklist to serve as a reminder to the recruiters of the steps required in the surgery in an attempt to reduce the extent of incomplete data collection.

10.1.6 Sample size to assess mandibular growth

Another limitation to this study was that only 36 of the patients who were in the final analysis, had two lateral cephalograms taken by the end of the data collection period. This meant that when measuring mandibular growth, the sample size was only 36. When this is broken down further into the different CVM stages, there were only 5 patients in the CVM stage 1 and 2 group, and only 12 patients in CVM stage 5 and 6. Due to the small numbers involved, it was not possible to show any significant differences, even though some patterns could be seen in the differences in mandibular growth at each CVM stage. The data could therefore, only be described using the means, and these should be interpreted with caution due to the small numbers involved.

10.1.7 Measuring mandibular growth

There was much discussion on how best to measure mandibular growth. Various methods which have been described in the literature, were considered as discussed in section 2.6. However, regardless of how accurate or reliable the landmarks were that were measured (Co-Gn-Go), it is debatable as to how much this triangle actually represents real mandibular growth. Although cephalometric radiographs have been used extensively in orthodontic research to assess mandibular growth, it must be remembered that a cephalogram is a magnified two-dimensional image of a three-dimensional object. There are many errors associated with landmark identification, constructing linear measurements, and the measurement of linear and angular structures.¹³⁴ Baumrind and Frantz¹³⁴ suggested that the observed difference as a result of therapy should be at least twice the standard deviation of the estimating error, in order to be sure that the observed difference was a biological one rather than a measurement error. This suggestion appears reasonable when it is remembered that for each linear measurement, two estimations are being made thus there are two opportunities for errors to arise. Taking this into account, together with the knowledge that condylion is particularly prone to landmark identification error, the limitations of cephalometrics must be considered very critically when assessing cephalometric data. It has been suggested that three-dimensional radiographic imaging with cone-beam computed tomography (CBCT), that allows quantitative and qualitative analysis of bone is the only thing that can precisely measure the amount and direction of mandibular growth that has occurred.⁸³ Clearly this was not something that could be considered in this study due to ethical contraindications of exposing patients to excess radiation.

When considering the results from analysis of mandibular growth, it is important to interpret non-significant results with care. Lack of evidence of a difference in effect does not necessarily mean that there was no difference in effect.¹³⁵ It is important to recognize the patterns shown whilst recognising that these means are based on very small numbers. Further efforts will be made to gather these data as the patients within the study finish their orthodontic treatment.

10.1.8 Sample

The sample was taken from the patients being taken on for treatment from the orthodontic treatment waiting list. This included only patients who had been assessed and deemed appropriate for treatment under the NHS and within a hospital department. This may reduce the generalisability of the results, but as all patients were enrolled regardless of sex, skeletal classification or dental anomalies, this should have reduced bias. All ethnicities were included in the sample and this is a key difference between this sample and the sample from

the University of Michigan Growth Study. This may be a reason as to why the growth rates at CVM stages 1,2 and 5,6 were lower than the growth rates observed in the Franchi study, if there is a substantial variation in growth velocities in different ethnic groups. However, although data regarding participants' ethnicity was not collected, anecdotally the majority of the sample was Caucasian, so it is unlikely that the ethnic diversity of the sample was large enough to affect growth rates significantly.

10.2 Reliability Testing

One of the principal characteristics of an outcome measure is its reliability. Reliability refers to the reproducibility of the measurement when repeated at random in the same subject or specimen. The coefficient of reliability is an estimate of the proportion of all variation that is not due to measurement error and is readily estimated from replicate measurements. The reliability of a measurement determines its sensitivity and specificity and the power of a statistical test employing the measurement. All decline as the reliability of the measure declines. The reliability of a measurement is an important consideration in the choice of the primary outcome measure for a clinical trial. Reliability of measures should be assessed and assured by a quality control program based on randomly selected duplicate assessments.

With this in mind, inter-observer and intra-observer reliability was assessed for each of the three outcome measures i.e. CVM stage, statural height and cephalometric linear measurements.

10.2.1: Reliability of CVM Index

To assess the primary researcher's reliability in applying the CVM index, a selection of 72 images from patients at LUDH, in addition to ideal images provided by Professor J. McNamara, the co-author of the index, were assessed. This was done on two occasions 4 weeks apart to determine intra-observer reliability. In addition, SH's results were compared to JH's results to assess inter-observer agreement and to calibrate SH in the use of the index.

Agreement was assessed using Cohen's weighted kappa. Cohen's kappa coefficient is a statistical measure of inter-rater agreement for categorical data. It is generally thought to be a more robust measure than simple percentage agreement calculation since kappa takes into account the agreement occurring by chance. The kappa value was rated according to the scale described by Landis and Koch,¹³⁶ as demonstrated in Table 10.1. Other scales have been described such as that by Fleiss's arbitrary guidelines¹³⁷ (shown in Table 10.2). In

order to make the agreement data comparable to previous research²⁷, the scale described by Landis and Koch¹³⁶ was used.

Kappa Value	Agreement
<0	No agreement
0-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1	Almost Perfect

Table 10.1: Rating scale of kappa value described by Landis and Koch.¹³⁶

Fleiss's Arbitrary Guidelines	Agreement
<0.40	Poor
0.40-0.75	Fair to Good
>0.75	Excellent

Table 10.2: Rating scale of Fleiss's arbitrary guidelines.¹³⁷

There was discussion over how to set the weightings when measuring inter- and intra-observer agreement. Previous research has often given equal weightings to all categories so that if an observer is two categories away this is penalised twice as much as if they are one category away. On exploring the clinical implications of the weightings with regards to the CVM index, it was felt that an exponential weighting was more appropriate, so that if the observer is only one category off, the penalty is much less than if they are two categories away. This is because, despite the data being categorical, growth and indeed the change in shape of the vertebrae are continuous. In some cases the vertebrae are clearly defined as being a certain stage, however, there are instances where others are more difficult to assess, and are on the borderline of two stages. In this case, if a patient was a late stage 4 and was staged as an early Stage 5, then it was felt that this should be penalised less than if the patient was, for example a Stage 4 and staged as a Stage 6. Thus, an exponential weighting scale was used, when calculating the kappa values, as shown in Table 10.3.

The impact that the different weightings would have on the kappa value was explored and Table 10.3 shows an example of this for the inter-observer agreement between SH and JH using the 72 image sample of lateral cephalograms from LUDH.

Cohen's Weighted Kappa	Weighted by: $1-\text{abs}(i-j)/(1-k)$						Weighted by: $1-[(i-j)/(1-k)]^2$					
Ratings weighted by	1	0.8	0.6	0.4	0.2	0	1	0.96	0.84	0.64	0.36	0
Observed Agreement	92.5%						97.4%					
Kappa	0.76						0.84					
Interpretation	Substantial Agreement						Almost Perfect Agreement					

Table 10.3: Demonstration of different kappa value and agreement with different weightings assigned to categories

The Kappa statistic using equal weightings was 0.76 (92.5% observed agreement), which falls under the 'substantial agreement' category. The kappa statistic when the exponential weightings were used increased to 0.84 (97.4% observed agreement), which raises the level of agreement to 'almost perfect'. This demonstrates the importance of using the most appropriate weightings. This will of course depend on the measure being assessed. In this situation for the CVM index, it was felt that the exponential weightings were more appropriate when taking into account the clinical implications.

The intra-observer agreement had a kappa statistic of 1 (100% observed agreement); this falls under the 'almost perfect' category. The inter-observer agreement between researchers SH and JH was 'almost perfect', with an observed agreement of 97.4% K_w 0.84 SE (0.11) agreement. When comparing this to previous research, the most comparable study was the work done by Rainey,²⁷ as the setting and training was the same as that which SH followed. In addition, whole lateral cephalograms were used rather than cropped images, and the vertebrae were not traced, in order that the setting was as relevant to the clinical setting as possible. The intra and inter –observer reliability of the researchers BJ and JH was 'almost perfect' with kappa values ranging from 0.80-1, which is comparable to the agreement of the researchers in this study. When looking at the overall agreement of the other clinicians in Rainey's study, the agreement was 'substantial' with the mean intra-observer agreement being 0.70 and mean inter-observer agreement 0.67.²⁷ Thus, the agreement in the current study was higher than the average clinician who had not previously used the index, but was similar to the researchers involved. This would agree with Rainey's results that suggested that the amount of experience an observer had in using CVM, had a substantial impact on inter-observer reliability. This was demonstrated by the fact that the inter-observer reliability

for both the researchers in this study and in Rainey's study, was in the 'perfect agreement' category. However, the inter-observer reliability for the other researchers was only 'substantial'.²⁷

10.2.2: Reliability of Statural Height Measurement

The standing height of the patients in the study was carried out as recommended in the Tanner Whitehouse growth charts.⁶³ The patients were positioned with their feet together, flat on the ground, with their heels touching the wall. Their legs were straight, with their buttocks against the wall and their arms loosely by their side. The patient's head was positioned with the lower margins of the orbit in the same horizontal plane as the external auditory meati, i.e. with the Frankfort plane parallel to the floor.

The reliability of all of the StRs was classified as excellent, with the intra-class correlation coefficients for intra-observer agreement ranging from 0.993 to 0.997. The inter-observer agreement was 0.986; this was also classified as 'excellent' agreement. All of the Bland and Altman plots showed that the spread of the data was on the whole random, suggesting that there were no systematic errors of over or under measuring. Whilst there were outliers, there was usually no more than 1 per StR, which is probably inevitable in research of this type. In addition, the outliers were all within acceptable range from the limits of agreement.

The Bland and Altman limits of agreement was used, in addition to correlation coefficients, as this is increasingly being used to assess at agreement of linear measurements in the orthodontic literature and this makes these data more comparable.

The plot of difference against mean also allows any possible relationship between the measurement error and the true value to be investigated. The true value is not known, and the mean of the two measurements is the best estimate that could be obtained.¹³⁰

10.3: Assessing Mandibular Growth

The agreement when measuring condylion-gonion 4 weeks apart was 0.93 (intra-class correlation coefficient); this is classed as excellent agreement. The ICC was the same for gonion-gnathion at 0.93, also classed as excellent agreement. Agreement for gnathion-condylion was 0.85, this is classed as excellent agreement although it was lower than the agreement achieved with gonion-gnathion and gonion-condylion. A possible reason for this difference is that the primary researcher SH had as part of her normal practice regularly identified and used gonion as a cephalometric landmark. However, condylion and gnathion were two landmarks not commonly used previously; so it is interesting to note that the two

linear measurements containing gonion had a higher correlation coefficient than the measurement containing the two less familiar landmarks.

10.4 Findings: How They Relate to Previous Research

10.4.1: CVM Stage and Standing Height Velocity

The mean annualised growth velocity (MAGV) increased by approximately 5cm/yr from CVM Stage 2 to CVM Stage 3. It then reduced by 4cm/yr from CVM Stage 3 to CVM Stage 4. The MAGV further reduces by 3.5cm/yr between CVM Stages 4 and 5. All of the differences in the MAGV between the stages were found to be statistically significant ($p=0.001-0.009$) except between CVM stage 2 and 4, where there was no significant difference ($p=0.95$). It is perhaps surprising that the MAGV at CVM stage 1 and 2 wasn't lower as it was expected to have a similar velocity to CVM stage 5 and 6. However, when the numbers were broken down, there was only one patient at CVM stage 1 in that group; thus the MAGV primarily reflects the growth velocity of CVM stage 2 patients.

When comparing the results of this study, to the research that has been done previously in this area, the pattern of stature height growth velocity was similar to what Franchi et al.²⁰ found in their research as shown in Table 10.4. They also reported a statistically significant increase in MAGV from CVM stage 2 to 3 and a significant reduction from CVM stage 3 to 4 and again from CVM stage 4 to 5. However, some fundamental differences in the studies methodologies of the studies mean it is equivocal whether a direct comparison can be made. Firstly, Franchi et al.²⁰ only had 24 patients in their study, so it is questionable as to whether their sample size was sufficiently powered to draw any solid conclusions. There was no power calculation mentioned in the article and the reason for choosing the sample size was not discussed. In addition, their data were more longitudinal in nature whereas the results of this study were more cross-sectional in nature looking at patients over a CVM stage over a 1-year period.

Although the trend of the MAGV is the same in this study as that of Franchi et al.²⁰, there is a key difference in that the peak growth velocities are higher in the current study. This may reflect modern day diets. It is widely recognised that dietary habits have changed vastly over the last century due to a combination of factors, including innovation of technologies in kitchens, improved modes of transport systems, trade, migration and increased incomes. These factors have led to higher levels of fat and protein consumption in children today.¹³⁸ Variables that can be used to assess the effects of modernisation on health are summarised by Baker and Hanna (1986) and include increased body weight, physical growth and development and stature.¹³⁸

The sample used by Franchi et al.²⁰ was selected from the University of Michigan Elementary and secondary school growth study (UMGS). These patients were enrolled at the school from the mid 1930's to the late 1960's. Thus it is unsurprising that the current study shows a small increase in the MAGV in statural height compared to the figures quoted by Franchi et al.²⁰ However, it is surprising that these differences weren't larger given that the UMGS sample was selected 50-80 years ago. Even so, the data from the current study may reflect the changes explained by modernisation and change of dietary habits but will also have been influenced by the fact that the population treated in Liverpool is relatively deprived with 50% of patients falling within the lowest quintile of the Index of Multiple Deprivation (IMD) rating.¹³⁹ This suggests that a high proportion of patients included in the current study may have been from some of the most deprived areas in the UK. These issues highlight the importance of conducting research on a contemporary population, as this will give us a more accurate idea of how much growth can be expected in patients at each CVM stage but also suggest that other factors that contribute to growth need to be considered.

CVM Stage	Mean annualized growth rate (cm^y⁻¹) (LUDH n=108) 2014	SD	Mean annualized growth rate (cm^y⁻¹) (Franchi et al.²⁰ n=24) 1930-1960	SD	Mean Difference (cm^y⁻¹) [95%CI]
1 & 2	4.51	2.71	5.69	1.34	-1.18 [-2.69, 0.33]
3	9.39	4.44	8.70	1.7	0.69 [-1.52, 2.90]
4	5.00	2.33	4.96	2.1	0.04 [-1.87, 1.95]
5 & 6	1.56	2.34	3.35	1.78	-1.79 [-3.48, -0.10]

Table 10.4: Comparison of the MAGV from this study to Franchi et al. (2000) results

Table 10.4 and Figure 10.3 demonstrate the similarity in trend between the results of the current study and the work of Franchi et al.²⁰ Looking at the line graph in Figure 10.3, the peak growth velocity in the LUDH is slightly higher than the figure reported in the Franchi study. However, It is surprising that the growth velocity at CVM Stages 1, 2, 5 and 6 is higher in the Franchi et al. study than in the LUDH sample. It is difficult to say for certain why this is but again may be a reflection of the small sample sizes in each CVM group or differences in the populations measured with respect to time lag and socio-economic group. In order to provide more robust data, a much larger sample size, especially of patients in CVM stages 1&2 and 5&6, would be required and this could be the topic of future research.

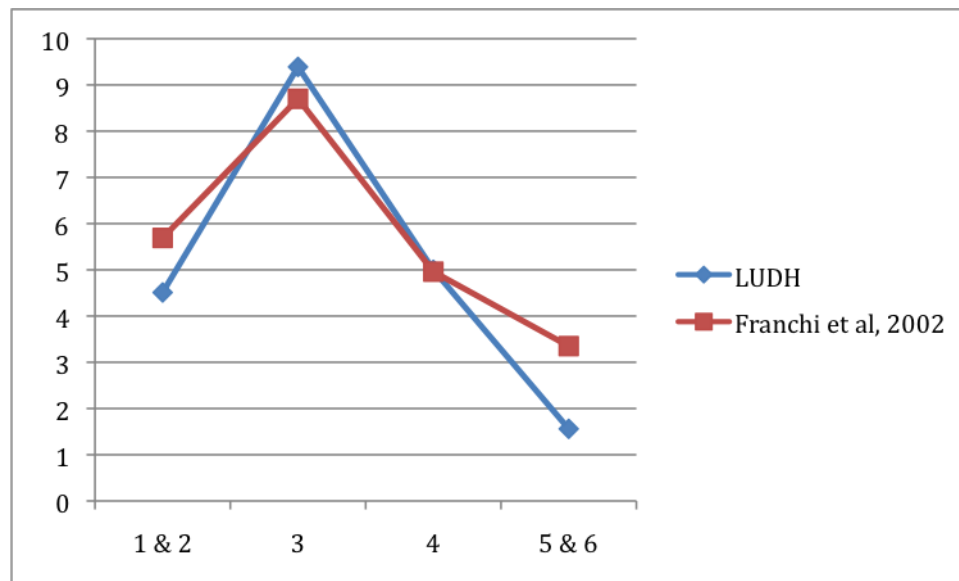


Figure 10.3: Line graph showing MAGVs at different CVM stages for this study and its comparison to the Franchi et al. (2000) study.

Mitani and Sato (1992) investigated growth of the mandible, in relation to cervical vertebral maturation and standing height.⁷³ They showed a consistent strong correlation between body height and cervical vertebrae, however, they presented their results in terms of chronological age rather than stage of cervical maturation stage thus a direct comparison is not possible.

As well as the strong correlation between CVM stage and standing height growth velocity, many authors have reported a strong correlation between standing height growth velocity and mandibular growth⁷³. Van der Beek et al⁷² showed that the growth velocity of standing height was a good indicator for mandibular growth velocity. However, different measures were used to assess mandibular growth so comparison with the current study is difficult. The parameters they used for mandibular growth were sella-gonion (S-Go) and nasion-gnathion (N-Gn). They found a stronger relationship with standing height growth velocity and S-Go than standing height and Na-Gn.

This confirms the work by Hunter,¹¹ Grave,¹⁴⁰ Moore et al,⁷¹ and Thompson et al,¹⁴¹ Hunter,¹¹ concluded that in 86% of their sample, maximum increments in mandibular growth were reached either coincident to (57%) or after (29%) the peak in standing height growth velocity. Lewis et al.¹⁴² found that periods of accelerated growth in ramus height coincided with those in standing height. In addition, Moore et al.⁷¹ also found the largest correlations for standing height was with sella-gonion.

Though these results are encouraging and their findings are corroborated by the results of this study, there is a significant gap in the research in this area. Prior to this study, research had usually been based on historical populations and conducted retrospectively. In addition, there is a large amount of variation in the parameters used to measure mandibular growth so any statistical comparison is difficult. Further research needs to be carried in this area and a standardised method of assessing mandibular growth, without the need for additional radiation exposure that the use of CBCT would involve, needs to be defined.

10.4.2: CVM Stage and Age

The results of this study showed that girls were reaching their peak growth spurt at an earlier age than boys. The average age of girls at CVM stage 3 was 12.4 years (age range 10.6-13.6 years, 95%CI 11.46;13.36) whereas the average age of boys at CVM stage 3 was 13.6 years (age range 11.8-14.5 years, 95%CI 13.06;14.09). This supports previous research, which reports that girls tend to have their peak in growth spurt prior to boys.^{13, 50-52} Franchi et al.²⁰ reported that at CVM stage 3, chronological age for females ranged from 8 years 6 months to 11 years 5 months, whereas for the boys it ranged from 10 years to 14 years. Thus, the authors argue that the differences in these age ranges demonstrate why chronological age cannot be used as a parameter for the appraisal of individual skeletal maturation and for the definition of treatment timing.

Recently, Beit et al.⁴⁷ suggested that CVM staging was no better at predicting the peak in growth than chronological age. However, their sample was taken from a retrospective growth study carried out in 1981. Furthermore, these data suggest that there was no significant difference in the ages between CVM stages 1-2, 3 and 4. This contrasts with mean annualised growth velocity, where a very significant difference was found between the different CVM stages. The findings of the current prospective study would therefore suggest that CVM is much more valid as a predictor of growth than chronological age.

When comparing the mean age at each CVM stage in the current study with the mean age at each CVM Stage in the Franchi et al.²⁰ study, it can be seen (in Table 10.5) that generally, the patients in the current study were older at each stage than in Franchi et al. This is perhaps surprising when the literature tends to suggest that children are tending to go through puberty at an earlier age currently than they did historically.

CVM Stage	Mean Age (Years) LUDH			Mean Age (Years) (Franchi et al ²⁰ n=24)		Difference (Years)
	Mean Age	95%CI		Mean Age	95%CI	
1 & 2	12.71	12.01	13.41	9.10	Data not available	2.91
3	13.15	12.65	13.65	10.67	Data not available	2.48
4	13.55	13.00	14.11	11.68	Data not available	1.87
5 & 6	15.23	14.76	15.70	13.25	Data not available	1.98

Table 10.5: A comparison of the mean age at each CVM stage from this study and from the Franchi et al.²⁰ study.

10.4.3: How Valid Are These Results?

The reliability results all show excellent inter-and intra observer agreement. The differences in MAGV between the CVM stages were statistically significant, with the p value ranging from 0.001 to 0.009. However, the sample size in the group containing CVM stages 1 and 2 was underpowered by 3 patients fewer relative to the original sample size calculation. However, despite this, the results were significant, so the number of participants was sufficient to detect a statistically significant difference. It is unlikely that these results and significance would have changed if 3 more patients had been in this group. An inadequate sample size is an issue when there is no significant difference, because it is unknown whether the result of no difference is due to the sample being underpowered or whether there is truly no difference. However, as the results of this study were highly statistically significant, on discussion with the statistician (G.Burnside) it was felt that the study was adequately powered.

10.4.4: CVM Stage and Mandibular Growth Velocity

The results assessing the mean rate of mandibular growth at the different CVM stages, as identified in Chapter 9, were inconclusive due to the small sample size. They will, therefore, be discussed with regards to the general trends displayed with the knowledge that firm conclusions cannot be drawn based on these data, and that a much larger sample size would be required to provide sufficient power to detect a significant difference.

The peak in mandibular growth occurred at two stages, CVM stages 3 and 4 where the mean annualised mandibular growth rate was $0.448\text{cm}^2\text{y}^{-1}$ and $0.446\text{cm}^2\text{y}^{-1}$ respectively. The rate was lower at CVM stages 1 and 2 at $0.192\text{cm}^2\text{y}^{-1}$ and again was lower at CVM stages 5/6 at $0.257\text{cm}^2\text{y}^{-1}$.

When an ANOVA test was carried out, to test the null hypothesis of no difference between the groups, no significant difference could be detected between any of the groups for the area of the triangle Co-Go-Gn or for any of the 3 linear measurements making up the triangle. This again, is likely to be due to the small sample size.

When the results of this research were compared to other research, looking at mandibular growth velocity at different CVM stages, the trend is comparable to other authors' work. The results of research looking at the velocity of mandibular growth in relation to CVM stage, are divided; some studies have found that peak mandibular growth velocity coincides with CVM stage 3 or peak standing height growth velocity.^{13, 33, 34, 71} However, there is also a body of evidence to suggest that the peak mandibular growth velocity occurs just after the peak in standing height growth velocity or after CVM stage 3 and this 'time-lag' effect has been documented many times in the literature.⁷⁰

O'Reilly et al.¹⁸ showed that the peak in mandibular growth occurred between CVM stage 3 and 4 as shown in Figure 10.4. The mean mandibular growth velocities on the graph at Stage 3 and Stage 4 are similar and are placed on the slope of the curve either side of the peak. This would explain the similar rates of mandibular growth at CVM stage 3 and 4 that were obtained in the LUDH study. However, in the O'Reilly et al.¹⁸ study, mandibular length was measured using articulare as a landmark. As discussed, it is controversial as to the accuracy of this landmark to assess mandibular growth. An increase in mandibular length can be presumed when the condyles are simply positioned more anteriorly within the glenoid fossa.

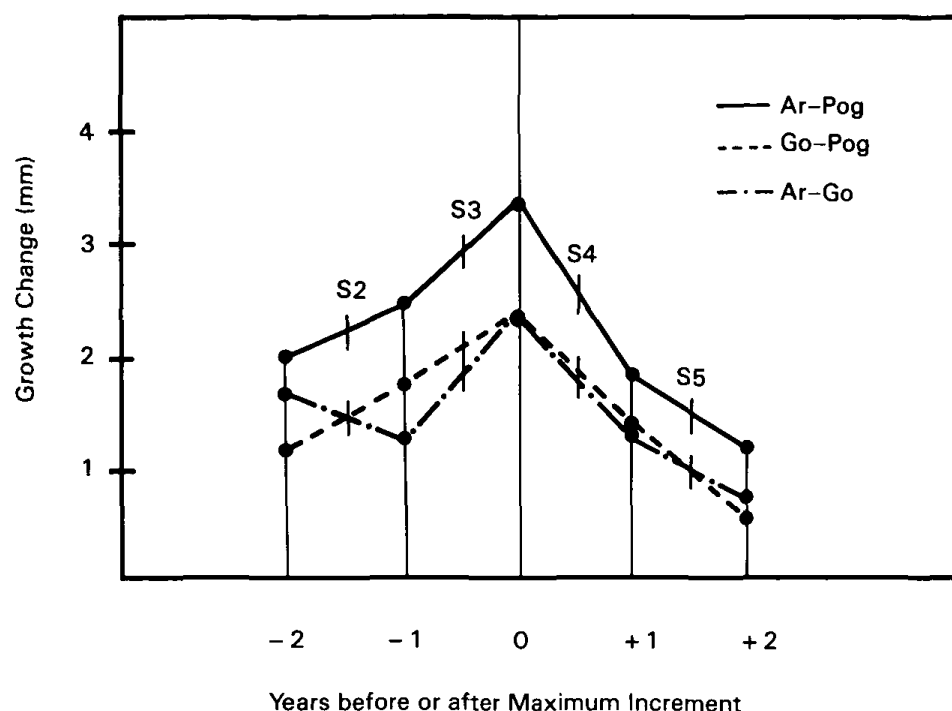


Figure 2

Average curves for mandibular length (Ar-Pog), corpus length (Go-Pog), and ramus height (Ar-Go) superimposed on maximum increment.

S2 vertebral stage 2

S4 vertebral stage 4

S3 vertebral stage 3

S5 vertebral stage 5

Figure 10.4: Mandibular growth at different CVM stages. Modified from O'Reilly et al¹⁸.

Hunter¹³ found that there was a relatively high correlation between the gain in length of the mandible and statural height in both males and females ($r=0.76$). The increase in the length of the mandible was also closely related to the growth in statural height during the adolescent growth spurt. They concluded that maximum facial growth was coincident with maximum growth in height in the majority of subjects in the study; furthermore, they concluded that the anteroposterior length of the mandible, of all facial dimensions, exhibited the most consistent relationship with growth in height throughout adolescence.¹³ However, these results do need to be interpreted with caution, as the sample was a sample of convenience that was not randomly selected and was obtained from the child research council, Denver Colorado. This was undertaken from the early 1930s and growth patterns as well as population demographics may have changed over the last eighty years.

More recently, Gu et al.¹⁴³ also reported that the peak in mandibular length was observed during the interval between CVM stage 3 and CVM stage 4 even though mandibular

remodeling and growth continued over a relatively long time period after the peak in mandibular growth had occurred.

Furthermore, Bergersen³³ reported that there was a significant correlation between the growth of all facial dimensions including mandibular growth and standing height. It was shown in his research that there was no significant difference between peak mandibular length growth velocity and peak standing height growth velocity.

Several other authors have also reported that the peak in mandibular growth velocity coincides with a peak in standing height growth velocity.^{13, 77}

Mitani and Sato⁷³ looked at the size of the mandible in relation to CVM stage, and found that they were strongly correlated up to the age of 11, but then this correlation weakened. Despite them reporting a significant correlation between standing height growth velocity and CVM, they found that the mandible showed substantial variation in its timing of peak growth. Despite this, it was reported that within a limit of a 1-year lag, the peak growth of the mandible coincided with peak growth of standing height in 73% of the sample and with CVM in 82% of the sample. Without the time lag, the timing of peak mandibular growth was not highly correlated to any parameter. However, to assess mandibular growth, they only measured condylion-gnathion. This may risk missing any mandibular growth that has occurred at gonion and within the mandibular ramus. It is therefore difficult to make a direct comparison of these results and those obtained in the current study, regarding mandibular growth due to the different parameter measured; this highlights the importance of more research in this field using standardized methodologies so that results are comparable.

Other research reported that the peak in mandibular growth velocity occurred slightly later than the peak in standing height growth velocity includes Fishman et al.,³⁸ who reported that the mandibular growth velocity peaked later than statural height peak velocity. In their research, it was found that statural height demonstrated a greater percentage of completed growth than mandibular and facial growth in mid-late adolescence. This pattern of a lag between statural height peak growth and mandibular peak growth has also been reported by other authors.^{35, 78}

Bacceti et al.¹⁶ reported that the peak in mandibular growth velocity occurred at CVM Stage 3, which differs slightly from the findings of the current study where the peak in mandibular growth seems to be concentrated at CVM Stages 3 and 4. However, it is equivocal as to whether a comparison can be made as in the Bacceti et al. study, they used records from the University of Michigan study, which, as discussed previously, is an historic sample, and the study was carried out retrospectively. Although the value of serial lateral cephalograms

and height measurements from the historic growth studies must not be underestimated, prospective longitudinal studies, using a contemporary population, are preferable on which to draw valid conclusions.

In summary, peak growth velocity in standing height has been shown to be one of the most accurate methods of determining the overall skeletal growth velocity. Despite the variations in the methodologies of the studies carried out previously in this area, a consistent positive relationship between peak in height and peak in mandibular growth, with or without a time lag, has been demonstrated. This suggests that mandibular growth peaks around CVM stages 3 to 4, which is consistent with the results of the current study, within the limitations regarding sample size.

10.5 Applicability of Results

The population from which the participants were recruited was those patients of two consecutive cohorts of registrars at LUDH, who ranged in age from 8 to 18 years old. Males and females were included from all ethnic backgrounds, undergoing all modalities of orthodontic treatment. This was in an attempt to increase the generalisability of the results. Patients diagnosed with any congenital clefts of the lip and/or palate, or known or suspected craniofacial syndromes or growth related conditions were excluded. This was so that any syndromic effects on growth did not confound the results.

Using a population from a dental hospital means that the results of this study may be applicable to the larger population that undergoes orthodontic treatment. The setting in an NHS Dental Hospital was common to many cities in the UK. Despite this, the fact that it was only set in the dental hospital in Liverpool may limit the generalisability of the results to some extent due to variations in the populations that attend for treatment around the UK. Ideally, the study could be expanded to include both primary and secondary care settings and potentially a multi-centre study so that the results would be generalisable nationwide.

The sample for the current study was a sample of convenience, as the aim was to recruit a large enough sample to detect a significant difference in the annualised growth velocity between the different participants at different CVM stages, with an 80% power at a p value of 0.05. However, the sample was not selected randomly, thus the risk of selection bias must be considered. Registrars were asked to recruit all patients who met the inclusion criteria and who consented to being in the study. It could be argued that the registrars, because they knew their patients, would make a decision whether to ask them or not, and may consciously or sub-consciously have introduced some selection bias. In addition, the sample was not balanced across the CVM stages.

10.6 Implications for Clinical Practice

- This method of assessment of CVM stage provides clinicians with information for assessing the timing of peak statural height growth and potentially peak mandibular growth.
- Growth is a critical variable in orthodontic treatment. A treatment plan can vary from involving orthognathic surgery to camouflage with the extraction of teeth to functional appliance treatment on a non-extraction basis, depending on a patient's growth potential. By assessing the cervical vertebrae on a lateral cephalometric radiograph, the orthodontist can now potentially evaluate the growth stage of the patient at that point in time. This will provide the orthodontist with a reasonable idea as to how much growth should be factored into anticipated treatment.
- With regards to treatment timing: patients being considered for functional appliance therapy can be assessed with regards to their current growth velocity and future growth potential.
- Patients being considered for surgical treatment or dental implants will have a clearer idea of the timing of their treatment based on an assessment of the amount of growth they have remaining
- As a lateral cephalometric radiograph is already routinely required for a full orthodontic assessment, this information is readily available to the orthodontist and will obviate the need for additional hand–wrist radiograph thus reducing radiation dose to the patient.

10.7 Implications for Future Research

- Further research into the velocity of mandibular growth at each CVM stage would be a logical step after this research. If clinicians knew how much mandibular growth could be expected at each stage, this may have a huge impact on orthodontic treatment planning. A larger sample size and longer study duration would be required.
- It would be of interest to conduct this research as a multi-centre, prospective study to assess whether the results are similar across the UK. The implications of validating the CVM method on clinical practice would be invaluable.
- It would also be valuable to examine the influence of ethnicity upon growth rates. As discussed, the ethnic mix of the sample in this study is likely to be more diverse than the sample used in Franchi et al's study and thus it would be insightful to account for this factor to see if this explained for the differences in growth velocities at CVM stages 1,2,5 and 6.

- In addition, the influence of the Index of Multiple Deprivation may have an effect on a participant's growth velocity. Liverpool is a diverse city, and many of the participants may come from deprived backgrounds and this may be a factor that affects growth velocity. A larger sample is likely to be required in order to assess the effect of the Index of Multiple Deprivation upon growth velocity.

Chapter 11: Conclusions

- The findings of this study demonstrate the validity of the cervical vertebral maturation (CVM) method for the identification of the pubertal peak in statural height growth rate with statistically significant differences being found in the mean annualised height growth rate between all the CVM stages except between Stages 2 and 4.
- The peak in statural height growth velocity occurred at CVM Stage 3 in both males and females.
- The females at CVM Stage 3 were significantly older than the males.
- The peak in statural height rate, at CVM Stage 3, occurred slightly ahead of the peak in mandibular growth rate, as assessed by the triangle condylion-gonion-gnathion, at Stage 3 and 4.
- No significant differences could be demonstrated between the CVM stages with regards to mandibular growth rate velocity due to the sample size.
- The CVM method can be used to augment other diagnostic tools available to the orthodontist, as it is already available on the lateral cephalogram.
- By assessing the CVM stage, the orthodontist can gain an idea of how much potential growth should be factored into the treatment plan.

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Appendix 1: Participant Information Leaflet



Department of Orthodontics
Liverpool University Dental Hospital and School of Dentistry
Pembroke Place, Liverpool L3 5PS

PARTICIPANT INFORMATION SHEET

Is cervical vertebral maturation (CVM) a good predictor of growth?

What is the purpose of the study?

As Orthodontists we regularly treat patients, like you, who are growing and maturing as they grow up from a child, to a teenager and then to an adult. Predicting how much patients will grow may affect the type of braces we offer them and the result they get from their treatment. Cervical vertebral maturation (CVM) is a measure taken from the neck bones on the X-ray pictures we use routinely as part of your treatment. Your orthodontists will check these as a routine part of their assessment process. Some research suggests that CVM may provide valuable information about growth, which may allow us to predict how much growth we can expect. This would then allow us to target treatment better and, potentially, reduce the length of orthodontic treatment.

Has the study been approved?

Yes. Liverpool Local Research Ethics Committee has given the approval for this study.

Who is paying for the study?

The School of Dental Sciences of the University of Liverpool is paying for the study. The Royal Liverpool and Broadgreen University Hospital Trust and the University of Liverpool are co-sponsoring the study.

Who will be conducting the study?

The study is being led by Dr Jayne Harrison (Consultant in Orthodontics) and carried out Sara Hosni, Ayeh Mahdmina, Andy Garry and Muneera Al-Mazyad (Specialist Registrars in Orthodontics).

Why have you asked me to take part?

We asked you to take part in this study because you are having orthodontic treatment and are still growing.

What will I have to do?

You will have your height measured at each of your routine orthodontic appointments. Your treatment will be different in **no** other way.

How long will the study last?

The study will last for the full length of your treatment.

What happens if I don't want to take part?

If you don't want to take part in the study, your treatment will continue as normal. You do not have to take part in the study and shouldn't feel you have to take part. If you don't want to take part in the study, you don't have to give us a reason. If you do take part in the study, but then decide that you don't want to carry on, you can withdraw at any time without giving a reason.

What if I have a question or there is a problem on the study?

If you have a concern about any aspect of this study, you or your parent(s) should ask to speak a member of the research team on 0151 706 5252. They will do their best to answer your questions. If you or your parents are still unhappy and wish to complain formally, your parents can do this through the Patient Advice Liaison service or by emailing; complaints@rlbuht.nhs.uk. Details can be obtained from http://www.rlbuh.nhs.uk/for_patients/Complaints_FAQs.asp

How will you collect and look after data (information) about me?

No one will be able to identify any of the data we collect about you. As soon as we have collected the necessary data, we will remove all information that identifies you and replace it by a code number. Only members of the research team will process and analyses your data. The person responsible for security and access to your data is Dr Jayne Harrison, the Co-Chief investigator of the Study. The data will be stored safely for ten years.

What do I do if I want to take part?

If you would like to take part in our study, please sign all the appropriate parts of the consent form that we will give you.

THANK YOU FOR TAKING THE TIME TO READ THIS LEAFLET

Appendix 2: Participant Consent Form



Centre Number:

Study Number:

Patient Identification Number for this trial:

CONSENT FORM

Title of Project: **Is cervical vertebral maturation (CVM) a good predictor of growth?**

Name of Researcher: Sara Hosni

Please initial box

1. I confirm that I have read and understand the information sheet dated January 2013 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that the data collected during the study will be analysed by the study investigators. I give permission for these individuals to have access to my records.

4. I agree to take part in the above study.

Name of participant

Date

Signature

Name of Person
taking consent

Date

Signature

Appendix 3: Parent/Guardian Information Leaflet



Department of Orthodontics
Liverpool University Dental Hospital and School of Dentistry
Pembroke Place, Liverpool L3 5PS

PARENT INFORMATION SHEET

Is cervical vertebral maturation (CVM) a good predictor of growth?

What is the purpose of the study?

As Orthodontists we regularly treat patients, like your child, who are growing and maturing as they grow up from a child, to an adolescent and then to an adult. Predicting how much patients will grow may affect the type of braces we offer them and the result they get from their treatment. Cervical vertebral maturation (CVM) is a measure taken from the neck bones on the X-ray pictures we use routinely as part of your child's treatment. Your child's orthodontists will check these as a routine part of their assessment process. Some research suggests that CVM may provide valuable information about growth, which may then allow us to predict how much growth we can expect. This would then allow us to target treatment better and potentially, reduce the length of orthodontic treatment.

Has the study been approved?

Yes. Liverpool Local Research Ethics Committee has given the approval for this study.

Who is paying for the study?

The School of Dental Sciences of the University of Liverpool is paying for the study. The Royal Liverpool and Broadgreen University Hospital Trust and the University of Liverpool are co-sponsoring the study

Who will be conducting the study?

The study is being led by Dr Jayne Harrison (Consultant in Orthodontics) and carried out by Sara Hosni, Ayeh Mahdmina, Andy Garry and Muneera Al-Mazyad (Specialist Registrars in Orthodontics).

Why have you been asked my child to take part?

We asked your child to take part in this study because he/she is having orthodontic treatment and is still growing.

What will I have to do?

Your child will have his/her height measured at each of their routine orthodontic appointments. Their treatment will not be different in any other way.

How long will the study last?

The study will last for the full length of your treatment.

What happens if I don't want to take part?

If you don't want your child to take part in the study, his/her treatment will continue as normal. Your child does not have to take part in the study and you shouldn't feel you have to let them take part. If you don't want your child to take part in the study, you don't have to give us a reason. If your child does take part in the study, but then you decide that you don't want them to carry on, you can withdraw your child at any time without giving us a reason for doing so.

What if I have a question or there is a problem on the trial?

If you have a concern about any aspect of this study, you should ask to speak to a member of the research team on 0151 706 5252. They will do their best to answer your questions. If you are still unhappy and wish to complain formally, you can do this through the Patient Advice Liaison service or by emailing; complaints@rlbuht.nhs.uk. Details can be obtained from http://www.rlbuht.nhs.uk/for_patients/Complaints_FAQs.asp

How will you collect and look after data (information) about my child?

No one will be able to identify any of the data we collect about your child. As soon as we have collected the necessary data, we will remove all information that identifies your child and replace it by a code number. Only members of the research team will process and analyses your child's data. The person responsible for security and access to your child's data is Dr Jayne Harrison, the Co-Chief investigator of the Study. The data will be stored safely for ten years.

What do I do if I want to take part?

If you would like your child to take part in our study, please sign all the appropriate parts of the consent form that we will give you.

THANK YOU FOR TAKING THE TIME TO READ THIS LEAFLET.

Appendix 4: Parent/Guardian Consent Form



Centre Number:

Study Number:

Patient Identification Number for this trial:

CONSENT FORM FOR PARENT/LEGAL GUARDIAN

Title of Project: **Is cervical vertebral maturation (CVM) a good predictor of growth?**

Name of Researcher: Sara Hosni

Please initial box

1. I confirm that I have read and understand the information sheet dated January 2013 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that the data collected during the study will be analysed by the study investigators. I give permission for these individuals to have access to my child's records.

4. I agree for my child to take part in the above study.

Parent/Legal guardian

Date

Signature

Name of Person
taking consent

Date

Signature

Appendix 5: Child Assent Form



Department of Orthodontics
Liverpool University Dental Hospital and School of Dentistry
Pembroke Place, Liverpool L3 5PS

INFORMATION SHEET AND ASSENT FORM

We want to tell you about a research study we are doing. A research study is a special way to find out about something. We are trying to find out more about growing up. You are being asked to join the study because you are growing.

Why are we doing this study?

We treat lots of patients, like you, who are growing up. Knowing how much patients will grow might change what type of brace we give and how well the brace works. We can learn about growth by looking at the x-ray pictures we took of you. We can also learn more about it by measuring your height.

Why have you asked me to take part?

We asked you to take part in this study because you are wearing a brace and you're still growing.

What will I have to do?

We will measure your height every time you come to see us. This is the only extra thing we will do for the study.

Do I have to take part?

No, you don't have to be in the study. It's up to you. If you say yes now, but you change your mind later, that's okay too. All you have to do is tell us.

Can anything good happen to me?

It won't change your brace treatment. But we hope to learn something that will help other children one day.

How long will the study last?

The study will last until you finish your braces come off.

Will anyone know I am in the study?

We won't tell anyone you were in this study. When we have finished the study, we will write a report about



what we found out. We won't use your name in the report.

What if I have a question or there is a problem on the study?

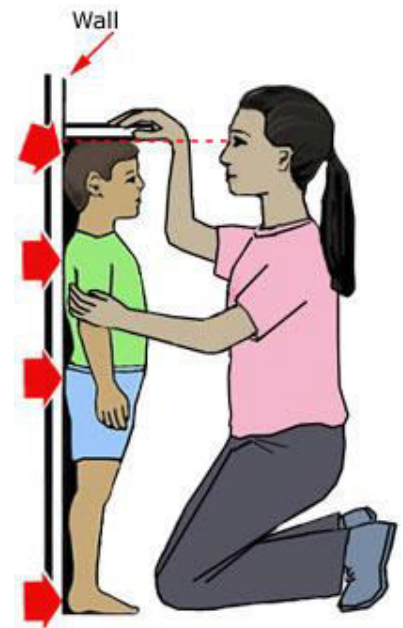
If you have a question about the study, or if you are worried about anything, you or your parent can ask me when you come to have your brace checked.

What do I do if I want to take part?

If you want to be in this study, please sign or print your name on the next page.

Assent

1. I have read and understand the information about the study. I have asked any questions I wanted to and these have been answered.
2. I understand that I don't have to be in the study and I can change my mind any time without giving a reason.
3. I understand that the research team will be looking at my height and x-ray pictures. I give permission for them to look at my records.
4. I agree to take part in the above study.



Name of participant Date Signature

Name of Person Date Signature
taking assent

THANK YOU FOR READING THIS LEAFLET

Appendix 6: Standing Height Table

Patient
Sticker



Weight at first appointment:

Date	Standing Height (cm)